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TRANSACTIONS OF THE

Chicago Pathological Society

From June 1, 1919, to June 1, 1923

VOLUME XI

AMERICAN MEDICAL ASSOCIATION PRESS
CHICAGO: NINETEEN HUNDRED TWENTY-THREE

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Seufert, E. C.....April 27, 1921
Quine, William E.....Dec. 7, 1922

INDEX OF SUBJECTS AND NAMES

PAGE

Abortion or miscarriage, bacteriology of systemic infections causing death following 279
Abscess of the brain arising from septic endocarditis 19
Abscesses, multiple of the brain secondary to bronchiectasis and Kyphoscoliosis 66
Acid-fast organisms, cultural difference among 266
Adenocarcinoma, mammary, a case of with peculiar reaction to the glands of internal secretion 295
Adenoids, diphtheria and diphtheroid bacilli of 225
Adenoids, fusiform bacilli and spirochetes in 385
Adenoids, streptococci and pneumococci of 173
Adenoids and tonsils, influenza bacilli of 179
Agglutination of bacteria by immune serum, hydrogen ion changes with 289
Agglutination of human erythrocytes by horse serum 46
Alcohol and nicotin, influence of on the ovary 59
Albuminuria, summary of observations in tests for 57
Anaphylactic shock, changes in the reaction of the blood during 251
Anaphylactic and peptone shock, on the fundamental physiologic reaction in 98
Anaphylaxis, new studies in 392
Aneurysm, dissecting of the aorta 233
Aneurysm, healed dissecting of the abdominal aorta 133
Aneurysm of the ascending aorta, rupture of into the superior vena cava 217
Aneurysm of the coeliac axis and abscess of the brain arising from septic endocarditis 19
Aneurysm of the interventricular septum of the heart with heart block 226
Aneurysm of the root of the aorta and its relation to coronary circulation 53
Aneurysm of vertebral artery 232
Animal parasite, acquired immunity to 18
Anthrax, hemorrhagic meningoencephalitis in 104
Antibody production, rôle of ommentum of rabbits and dogs in 399
Aorta, abdominal, healed dissecting aneurysm of 133

PAGE

Aorta, aneurysm of the ascending rupturing into the superior vena cava 217
Aorta, aneurysm of the root and its relation to coronary circulation 53
Aorta, congenital hypoplasia of root and arch of, and of the left ventrical 369
Aorta, dissecting aneurysms of the aorta 233
Arthritis, gonorrheal, serologic observations on 294
Asthma, bronchial, the pathological histology of the lung structure in 128

B. Coli, serologic and biologic relations of from renal infections to strains isolated from feces and the cervix uteri 278
Bacillus enteritidis peritonitis with report of a case 373
Bacillus fusiformis, the life cycle of 396
Bacon, Charles S. 143
Bartelmez, George W. 120
Bassoe, Peter 63, 211
Beck, Emil G. 249
Beeson, B. Barker 306
Bender, Lauretta 256
Bile duct, primary carcinoma of 21
Bismuth paste tumors 339
Bladder wall, chronic dissecting suppuration of secondary to a small abscess in the hypertrophied middle lobe of the prostate gland 153
Blood alkali reserve and leukocytosis, changes with experimental infections 171
Bone, relation of myeloma to multiple vascular tumors of 151
Bone and callus, multiple and bilateral traumatic parostial formations of femurs and left innominate bone .. 356
Bones, diffuse osteoplastic carcinoma of 63
Bowel, relation of to B. Coli kidney infections 348
Brain, abscess of arising from septic endocarditis 19
Brain abscesses, multiple secondary to bronchiectasis and Kyphoscoliosis 66
Brain, a green-producing cocus from, in a case of encephalitis 70
Brams, J. 292, 385
Brams, William A. 363, 406
Branham, Sara E. 251
Bronchiectasis and Kyphoscoliosis, brain abscesses secondary to 66

Buchbinder, William C..... 246

Carcinoma, diffuse osteoplastic of bones..... 63
Carcinoma, primary of the male urethra..... 365
Carcinoma, primary of the main hepatic bile duct..... 21
Carcinoma, squamous cell, the occurrence of in mice.... 205
Carcinoma of the cerebellum with syndactylism of the hands and feet..... 7
Carcinoma of the esophagus perforating into the trachea 380
Carcinoma of the lung, primary..... 326
Carcinoma of the small intestine..... 322
Carey, Eben J..... 356
Cary, William E..... 409
Cerebellum, carcinoma of with syndactylism of the hands and feet 7
Cerebral hemispheres, on the relation of to arterial blood pressure and body temperature regulation..... 115
Cerebrospinal fluid, precipitin index of with antihuman serum 136
Chardoma, sacrococcygeal 300
Chemical composition, relation of to immunologic specificity 203
Chorio-epithelioma of the testicle..... 61
Coccidioidal granuloma, demonstration of specimen of.. 320
Coeliac axis, aneurysm of and abscess of the brain arising from septic endocarditis..... 19
Colitis, polypoid, as a late stage of amebic dysentery.... 386
Colostrum, the function of..... 258
Coronary circulation, relation of aneurysm of the root of the aorta to..... 53
Crooks, T. T..... 361
Crowell, Dean P..... 233

David, Vernon C..... 348
Davis, D. J..... 201, 293, 320
Day, L. Enos 274
DeWitt, Lydia M..... 248, 256
Diabetes, with post-traumatic calcification of the pancreas 255
Diet, carbohydrate, on the protective action of on certain intoxications 1
Diphtheria and diphtheroid bacilli of the adenoids..... 225
Dog, hemolytic streptococci in the throat of..... 8
Ducrey Bacillus Infection (Chancroid) of the face..... 201
Ductus arteriosus Botalli, persistent patency of..... 290
Ductus arteriosus, patent, complicating acute anterior poliomyelitis 361
Dysentery, amebic, polypoid colitis as a late stage of.... 386

PAGE

Echinococcus disease of the kidney, report of a case.... 286
Ecuador, national and international relations of sanitation in 9
Egdahl, Anfin 206
Elliott, Charles A..... 14
Encephalitis, observations on a green-producing coccus from the brain in a case of..... 70
Endocarditis, septic, an unusual case of aneurism of the coeliac axis and abscess of the brain arising from.. 19
Endothelioma, meningeal, a case of simulating a tumor of the hypophysis..... 303
Erythrocytes, human, agglutination of by horse serum.... 46
Esophagus, carcinoma of perforating into the trachea... 380
Esophagus, a case of spontaneous rupture of..... 23

Foramen Ovale, patent..... 220
Fusiform bacilli and spirochetes in preputial secretions.. 292
Fusiform bacilli and spirochetes in tonsils and adenoids.. 385

Gallbladder, fatal hemorrhage from eroded arteria cystica of 394
Garcia, O. 293
Gonococcus, a simplified plate method of partial oxygen tension in the cultivation of..... 113
Gonococcus infection in the male, cultural and serologic observations of 178
Gummas of the base of the heart with syphilis of the aorta 300

Hassin, George B..... 211
Heart, aneurysm of the interventricular septum of with heart block 226
Heart, gummas of the base with syphilis of the aorta.... 300
Heart valves, two cases of congenital malformation of.. 345
Heart, with congenital patent interventricular septum... 156
H'Doubler, F. T..... 261
Hektoen, Ludvig 57, 60, 126, 221, 349
Heredity, influence of in determining tumor metastasis... 229
Herrold, Russell D..... 113, 178, 278, 294, 372
Herzog, Maximilian Joseph, life and works of..... 143
Hibbs, William G..... 49
Hines, Laurence E..... 386
Hirsch, Edwin F..... 74, 76, 105, 171, 172, 251, 289, 300
Holmes, Harriet F..... 75, 205, 337, 407
House, S. John..... 70, 104
Howell, Katharine M..... 317

PAGE

Huber, Harry L. ... 128
Huber, G. Carl ... 25
Hughes, T. P. ... 392
Hydrogen ion changes with the agglutination of bacteria by immune serum ... 289
Hydrogen ion concentration, factors influencing the final in bacterial cultures ... 85
Hydronephrosis congenital bilateral ... 105
Hypophysis, some lesions of ... 183
Hypophysis, tumors of ... 87

Immunity, acquired to an animal parasite ... 18
Influenza bacillus, the immunologic reactions of five strains isolated from a case of meningitis ... 211
Influenza bacilli of the adenoids and tonsils ... 179
Ingals, Mary ... 300
Intestine, small, carcinoma of ... 322
Intestinal tract, invasion of body by bacteria from ... 355
Intoxications, on the protective action of carbohydrate diet on certain ... 1
Irons, Ernest E. ... 135, 355

Jackson, Harry ... 61
Jackson, Leila ... 100
Jaffe, Richard H. ... 384, 392, 394
Joints, the pathology of loose bodies in ... 264
Jones, Horry ... 85

Kendall, Arthur I. ... 9
Kidney, echinococcus disease of ... 286
Kidney and adrenal, primary spontaneous tumors of in mice ... 337
Kidney, fusion dystopia of with genital anomaly ... 195
Kidney, relation of bowel to B. Coli infections of ... 348
Klemperer, Paul ... 284, 295
Koessler, Karl K. ... 128
Kottmann reaction for thyroid activity ... 261
Kraft, Adolph ... 150
Kretschmer, Herman L. ... 286, 365

Laibe, J. E. ... 261
Lederer, Francis L. ... 339
Lens, the specific precipitin reaction of ... 221
Leukocytosis and blood alkali reserve changes (Van Slyke) with experimental infections ... 171

PAGE
LEVINSON, S. A. 162, 261, 277, 392
LEWIS, JULIAN H. 258
Lipins of tubercle, grass and colon bacilli and liver tistue, changes produced by 352
Lipoma of the sigmoid, a case of 297
Lipocarcinoma, retroperitoneal 74
Liver, changes in mushroom poisoning 284
LONG, ESMOND R. 266
Lung, effects of the mode of death on changes in, in rabbits and guinea-pigs 251
Lung, primary carcinoma of 326
Lung, rhabdomyoma of in a sheep 274
Lymphosarcoma, marked blood changes accompanying 76

MATHERS, CAPT. GEORGE SCHRADER 60
Megacolon, report of a case in an adult 246
MCGILL, E. C. 348
Meningoencephalitis, hemorrhagic in anthrax 104
MEYER, JACOB 180
MEYER, KARL A. 363
Mice, primary spontaneous tumors of the ovary in 75
Mice, primary spontaneous tumors of the kidney and adrenal in 337
Mice, squamous cell carcinoma in 205
MILLER, NEWTON 300
Miscarriage or abortion, bacteriology of systemic infections causing death following 279
MOODY, WILLSON B. 135, 279, 355
Mushroom poisoning, liver changes in 284
Myelitis and myelomalacia 211
Myeloma, relation to of multiple vascular tumors of bone 151
Myelomalacia and myelitis 211

Nasopharynx, the flora of in tonsillectomized and non-tonsillectomized children 180
Neoplasm, malignant, an analysis of 545 cases of observed at postmortem examination, with reference to relation of clinical and anatomical diagnosis 371
Nerves, peripheral, transplantation of 25
Nervous system, sympathetic, studies on 125
NEYMANN, CLARENCE A. 136
NICKEL, ALLEN A. C. 373
Nicotin and alcohol, effect of on the ovary 59

PAGE

Oberhelman, H. A. 53
Ogata, Sukemasa 59
Omentum of rabbits and dogs, rôle of in antibody production 399
Ovary, preliminary studies on the influence of alcohol and nicotin on 59
Ovary, primary spontaneous tumors of in mice 75

Pancreas, post-traumatic calcification of, with diabetes .. 255
Paratyphoid B. bacillus, a guinea-pig epizootic due to ... 317
Pathology, a plea for the development of 309
Pearlman, S. J. 173, 179, 180
Pember, A. H. 226
Peptone and anaphylactic shock, on the fundamental physiologic reaction in 98
Peritonitis, bacillus enteritidis with report of a case 373
Petersen, W. F. 162, 261, 277, 392
Peterson, A. J. 261
Phemister, D. B. 264
Photographs, stereoscopic "Lumiere," a method of recording specimens in their fresh state by means of 249
Pilot, I. 173, 179, 180, 225, 292, 385, 406
Plasma, the relative toxicity of fetal and maternal 277
Poliomyelitis, acute anterior, patent ductus anteriosus complicating 361
Portis, Bernard 303, 326, 399
Portis, Sidney A. 297, 322, 380
Potts, H. W. 201
Precipitation test for syphilis of spinal fluid 372
Precipitin index of the cerebrospinal fluid with antihuman serum 136
Prostate gland, small abscess in the hypertrophied middle lobe of, primary to chronic dissecting suppuration of the bladder wall 153
Protozoan parasite, intracellular, of ducts of the salivary glands of the guinea-pig 100
Pyelitis and ureteritis cystica, hyperplastic 49

Ranson, S. Walter 125
Raulston, Burrell O. 63
Ray, Leighton W. 352
Retinger, J. M. 57
Reuling, F. H. 18
Rhabdomyoma of the lungs of a sheep 274

PAGE
Rigor Mortis in smooth muscle..... 172
Rogers, F. T..... 115
Russum, B. C..... 153

Sachs-Georgi reaction for syphilis..... 162
Saelhof, Clarence C..... 66
Salivary glands of the guinea-pig, intracellular protozoan parasite of the ducts of..... 100
Sarcocarcinoma of the uterus..... 384
Sarcoma, spindle-cells, intravascular..... 206
Scarlet fever, hemolytic streptococci in the stools of patients with 135
Schulhof, Kamil 349
Schultz, Oscar T..... 185, 195, 211, 309, 317
Semerak, C. B..... 87
Sherman, Hal W..... 8
Shipman, James S..... 352
Sigmoid, a case of lipoma of..... 297
Simonds, J. P..... 1, 98, 183, 345
Slye, Maud 75, 205, 229, 337, 407
Smith, E. L..... 320
Stangl, Fred H..... 21, 217, 220, 226
Stevens, H. C..... 7
Stomach, an unusual form of ulceration of..... 406
Streptococci, hemolytic, on the occurrence of in the stools of scarlet fever patients..... 135
Streptococci, hemolytic of the appendix vermiformis.... 150
Streptococci, hemolytic, in the throat of the dog..... 8
Streptococci and pneumococci of the adenoids..... 173
Sweany, H. C..... 19
Synapse, the morphology of in vertebrates..... 120
Syndactylism of the hands and feet with carcinoma of the cerebellum 7
Syphilis, gastric, a report of two cases studied anatomically 363
Syphilis, precipitation test of spinal fluid for..... 372
Syphilis, Sachs-Georgi reaction in..... 162
Syphilis of the aorta with gummas of the base of the heart 300
Sporotrichosis, sporo-agglutination in the diagnosis of.. 293

Testicle, chorio-epithelioma of..... 61
Testis, malignant tumors of..... 185

PAGE
Thyroglobulin, the precipitin reaction of..... 349
Tissue, growth of in vitro..... 409
Tongs, M. S..... 46
Tonsils and adenoids, influenza bacilli of..... 179
Tonsils, fusiform bacilli and spirochetes in..... 385
Tubercle bacilli, inhibitory action of some new mercury compounds on 248
Tuberculosis, blood changes in experimental..... 256
Tumors, bismuth paste..... 339
Tumors, malignant of the testis..... 185
Tumor metastasis, the influence of heredity in determining 229
Tumors, mixed, of the uterus..... 261
Tumors, primary spontaneous of the ovary in mice..... 75
Tumors, primary spontaneous of uterus in mice with a review of the comparative pathology of uterine neoplasms 407
Tumor, report of an intravascular, probably a spindle-cell sarcoma 206
Tumors of the hypophysis..... 87
Tunnicliff, Ruth 396

Ureteritis and pyelitis cystica, hyperplastic..... 49
Urethra, male, primary carcinoma of..... 365
Uterus, mixed tumors of..... 261
Uterus, primary spontaneous tumors of in mice with a review of the comparative pathology of uterine neoplasms 407
Uterus, sarcocarcinoma 384

Ventricle, left, congenital hypoplasia of and of root and arch of aorta..... 369
Vermiform appendix, hemolytic streptococci of..... 150
Vertebral artery, aneurysm of..... 232
Vertebrates, the morphology of the synapse in..... 120

Watkins, Richard W..... 23
Wells, H. Gideon.....
.....74, 75, 151, 203, 205, 232, 255, 258, 290, 337, 371, 407
Williams, J. Lisle..... 133, 251, 369
Wolf, Elizabeth Pauline..... 156

Xanthoma tuberosum multiplex, specimens from a case of 306

Yellow fever, clinical and pathological manifestations of 14

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TRANSACTIONS OF THE CHICAGO PATHOLOGICAL SOCIETY

VOL. XI. JUNE 1, 1919. NO. 1

ON THE PROTECTIVE ACTION OF CARBOHYDRATE DIET ON CERTAIN INTOXICATIONS

PRESIDENTIAL ADDRESS

J. P. SIMONDS

The agreeable privilege of presiding for a period over the meetings of the Chicago Pathological Society is also a coveted and highly appreciated honor. For the present year, this privilege involves responsibilities and duties not before confronted by the officers of this Society. These unique responsibilities cannot be met, even by our so highly efficient Secretary, without the full cooperation of every member. For, of the slightly more than one hundred seventy resident members, more than fifty, most of them our younger and most productive men, are in the service of our Country. Upon those of us who have remained at our accustomed work, there devolved the special duty, not only of maintaining the organization of the Society, but also, even in the face of multiplied tasks, of upholding the customary standard of our scientific programs. We await with keen anticipation the return of our absent colleagues with new ideas and renewed enthusiasm for research.

In a series of experiments carried out about three years ago, it was shown that the esterase content of the livers of dogs poisoned with phosphorus or with chloroform is not materially less than that of normal dogs, and that the feeding of liberal amounts of sugar causes an increase in the amount of this ferment in

both normal and phosphorus poisoned animals. In another series of experiments, using the same extracts as those just mentioned, it was found that phosphorus poisoning causes an appreciable reduction in the ereptic power of the liver, that the feeding of sugar does not increase the ereptase content of the livers of normal dogs, but that it does tend to prevent the diminution of this ferment when fed to animals poisoned with phosphorus. These findings have led to the formulation of certain ideas as to the mechanism of phosphorus poisoning, and of the detoxicating, antitoxic or sparing action of carbohydrate diet in poisoning with this substance. Inasmuch as the pathology of chloroform poisoning, acute yellow atrophy of the liver and eclampsia have much in common with that of phosphorus poisoning, what is said with reference to the mechanism of the latter and the effect upon it of carbohydrate diet, may, perhaps, be at least partially applied to those three conditions.

The conditions found in phosphorus poisoning may be summarized as follows: There is an increased catabolism of tissue protein as evidenced by changes in the division of urinary nitrogen, by the occasional excretion in the urine of amino-acids, especially leucin and tyrosin; and by the frequent presence in the urine of abnormal amounts of creatin and of increased amounts of creatinin. That the liver is the chief sufferer in this increased tissue destruction is shown by the absolute loss of weight and the decrease of protein and protein nitrogen in this organ, and by the presence in the liver of various products of proteid decomposition. There is, further, a marked increase of the fat in the liver, due in part to the unveiling of hidden or bound fat, and in part to the transport to the hepatic cells of fat which they are unable to burn. There is, in addition, a rapid and complete disappearance of glycogen from the liver. Finally, there is a diminution of intracellular ereptase with little or no change in the intracellular esterase.

That the presence of a useable carbohydrate may profoundly affect bacterial cellular metabolism has been demonstrated beyond peradventure by the experiments

of Kendall and his co-workers. The presence or absence of a readily available sugar also modifies the metabolism of animal cells as shown by the work of Landergren, Lüthje, Cathcart, Rolly, Lusk, and others. All of these investigators have presented evidence that the presence of a carbohydrate is absolutely essential for the endocellular synthetic processes in connection with protein metabolism. In view of this it is evident, therefore, that an augmented supply of sugar is needed in those conditions, like phosphorus poisoning, in which protein metabolism is definitely increased.

It is the liver which shows the most marked demonstrable lesions in phosphorus poisoning, and this organ is one of the most important storehouses of glycogen. It has been shown that the clinical symptoms are less severe and that the pathological changes in the liver are less marked in sugar-fed phosphorus poisoned dogs than in nonsugar-fed phosphorus poisoned dogs. Graham has demonstrated that the susceptibility of an animal to delayed chloroform poisoning is inversely proportional to the amount of glycogen in the liver. In its mechanism, this local protective action of glycogen may involve several factors. In the first place, the metabolism of the liver is increased in phosphorus poisoning along with that of the rest of the body, and the presence of an available carbohydrate will spare the protein of the liver cells.

Fischer sees in fatty degeneration a purely physicochemical phenomenon. Sugar is known to stabilize emulsions of fat. Hence the presence of an abundant supply of glycogen in the liver tends to prevent the "breaking" of the intracellular emulsion which is one of the factors concerned in fatty degeneration. Furthermore, sugar is among the substances which Bechhold and Ziegler found to exercise a retarding influence upon the diffusion of some other substances into gels.

Wells is of the opinion that in phosphorus poisoning there is an interference with the oxidative processes in the liver and that this accounts for the accumulation of fat in this organ in this condition. The glycogen present in the liver at the time of poisoning is rapidly

oxidized, for it quickly disappears from the liver without the occurrence of either hyperglycemia or glycosuria. It is possible, therefore, that the reduced oxidation in the liver may be due in part to the depletion of readily oxidizable substance. Rettig is of the opinion that the primary effect of phosphorus is not a direct toxic injury to the cells but that it is the result of the absence of easily oxidizable carbohydrate. In the effort to supply oxidizable material fat is brought to the liver in greater quantity than it is able to burn it. An adequate supply of readily oxidizable glycogen will, therefore, help to maintain the oxidative activity of the liver in the presence of any interference with intracellular oxidation due to phosphorus poisoning.

The metabolism of fats is not yet fully understood, but it seems probable that the intracellular lipases, which are related to, if not identical with, the esterases, synthesize fat in the cells from materials brought to them by the circulating fluids. Wells believes that in the presence of the inhibition of oxidation in the hepatic cells in phosphorus poisoning, the lipase synthesizes fat and he thus accounts for the accumulation of this substance in the liver. The observation recorded above that there is no reduction in the esterolytic activity of the liver in phosphorus poisoning harmonizes with this view. On the other hand, the observation recorded in the same paper, that the feeding of sugar increases the hepatic esterase in phosphorus poisoned dogs and that the livers of these sugar-fed animals showed less fatty change than did the controls, seems, at first sight, to be contradictory. But this is not necessarily true. In the oxidation of fats in the body it is probable that they are first hydrolyzed by the intracellular lipases. With the "sugar hungry" cells in phosphorus poisoning attracting an augmented amount of the crude materials from which fat is synthesized, the equilibrium point for the activity of lipase will be well toward the side of synthesis. The hydrolysis and subsequent oxidation of fats within the cells is therefore interfered with. The presence of easily oxidizable glycogen in the liver cells

reduces the demand for fat, so that the equilibrium point is not disturbed by the attraction of an excessive supply of raw materials.

The changes occurring in the liver in phosphorus poisoning have been very generally charged to the process of autolysis. Jacoby found that autolysis was very much more rapid in the livers of phosphorus poisoned than in normal dogs. Wells concluded that chloroform, phosphorus and possibly other poisons stop cell activity, leaving the autolytic enzymes free to digest the necrosed cells.

There is evidence that the amount of glycogen in the liver affects the rate of autolysis of that organ. The liver in phosphorus poisoning is free of glycogen, and, as just mentioned, undergoes very rapid autolysis. Schryver found that the autolytic processes were greatly accelerated in the livers of animals which had been given thyroid extract; and Kuriyama made the observation that the feeding of thyroid extract causes a rapid disappearance of glycogen from the liver. Bradley found that of the three types of muscle, skeletal muscle autolyzed most slowly while heart and smooth muscle autolyzed from 50 to 100 per cent. more rapidly. In this connection it may be noted that Cremer found 1.85 per cent. glycogen in skeletal muscle and 0.12 per cent. in heart muscle. Starvation frees the liver of glycogen. Lane-Clapon and Schryver found that not only was the latent period in autolysis much shorter in the livers of starved cats than in the livers of cats fed on the usual diet, but that the degradation of the proteid was more rapid and complete.

The effect of phosphorus poisoning in diminishing the amount of intracellular ereptase of the liver and of the feeding of sugar in preventing this reduction, has been mentioned. The function of intracellular ereptase is not fully understood, but since Vernon found it in all organs of the body, it appears probable that it is concerned with intracellular metabolism, most likely serving to synthesize amino-acids into peptones. The work of Folin supports this view. Bayliss has made it clear that "although the direct evidence on the subject of synthesis in protein metabolism is at present

meager, the phenomena seen in trypsin digests are quite what would be expected if equilibrium in a reversible reaction be the explanation of what takes place."

Van Slyke and Meyer have shown that amino-acids disappear very rapidly from the blood during digestion, being taken up and temporarily fixed by the tissues. Living cells do not normally contain demonstrable amounts of peptone. Hence the equilibrium point in the living cell is well on the side of the synthesis of amino-acids into peptone. Furthermore, the same cells contain tryptase and peptase so that any peptone synthesized by the ereptase is further synthesized by the associated intracellular enzymes into protein. Because the actual demand for nitrogen by the body is relatively small, the total amount of synthesis is not great, the major portion of the amino-acids stored in the tissues temporarily is ultimately eliminated as urinary nitrogen. It is only when the stored amino-acids are exhausted by starvation or by increased protein metabolism, as in phosphorus poisoning, that the equilibrium point is displaced to the side of intracellular peptolysis.

Schryver, who observed that the livers of starved animals autolyzed more promptly and more rapidly than did the livers of fed animals, has advanced the interesting idea that the liberation and activation of the autolyzing enzymes in the cells during life is a normal mechanism whose function is to protect the organism against starvation. These enzymes come into action only when the energy needs of metabolism are not satisfied by the foodstuffs ingested. Ereptase is only one of the enzymes concerned in autolysis. Hence it appears that in phosphorus poisoning, and probably in chloroform poisoning, acute yellow atrophy of the liver and in eclampsia, the normal activity of the intracellular enzymes including ereptase is reversed. The feeding of sugar and the resulting conservation and replenishing of the glycogen content of the liver tends to prevent the reversal of this activity.

We may conclude, therefore, that the conservation and replenishing of the glycogen of the liver by the administration of sugar, protects the animal against the toxic effect of phosphorus, (1) by its effect on the

colloids of the cell; (2) by furnishing the carbohydrate which is essential to the normal synthetic processes of protein metabolism; (3) by supplying the most easily oxidizable material to an organ whose oxidizing power has been reduced by the poison; (4) by inhibiting the process of autolysis *in vivo*; and (5) by preventing the reversal of the action of the intracellular enzymes.

January 13, 1919.

CARCINOMA OF THE CEREBELLUM WITH SYNDACTYLISM OF THE HANDS AND FEET

H. C. STEVENS

The patient, an unmarried white female, about sixty-five years of age, was admitted to the Chicago State Hospital, August 15, 1918. The history showed that she had been of normal mentality up to the commencement of her last illness. A tumor of the right breast and axilla had been first noticed seven years previously. Two years before being seen by the writer, a radical amputation of the right breast was performed. The first signs of cerebral trouble were nausea, vomiting and severe headache, dating back two years. Physical examination on admission to the hospital revealed complete blindness in both eyes, and absolute deafness in the right ear. The left ear was not entirely deaf. By shouting loudly in it she could be made to hear and by her replies to questions, it was apparent that she was disoriented as to time and place and considerably demented. Opthalmoscopic examination showed marked optic atrophy. The pupils reacted slightly and sluggishly to light. There was an intermittent spasm of all muscles supplied by the right facial nerve. These spasms were very intense, lasting from thirty to forty seconds and seeming to occur in groups, several recurring at intervals followed by longer periods of quiescence. The reflexes of the upper extremities were

brisk. The abdominal reflex was absent. The patellar reflexes were unchanged. The Babinski sign was present on the right side only. There was no ankle clonus. The patient was able to stand but could not walk. Speech was explosive and scanning in character. The patient had no control of either bladder or rectum. She died October 3, 1918. At autopsy, occupying the right hemisphere of the cerebellum, there was a hard growth palpable from the outside. On transverse section, the tumor was seen to occupy the center of the hemisphere. The center of the tumor was grayish in color, the periphery was reddish. Histologically the tumor was a carcinoma made up of a slightly developed stroma of connective tissue with large masses of carcinoma cells. In addition to the tumor of the brain, the patient had a peculiar symmetrical, syndactyly of all four extremities.

January 13, 1919.

HEMOLYTIC STREPTOCOCCI IN THE THROAT OF THE DOG*

HAL W. SHERMAN

From the John McCormick Institute for Infectious Diseases, Chicago

In view of the interest in hemolytic streptococci it seemed desirable to study the prevalence and characteristics of such streptococci in the throat of the dog.

Cultures were made by swabbing the throats of live dogs, endeavoring particularly to reach the tonsils and nasopharynx, and inoculating aerobic 10 per cent. goat blood-agar plates. Hemolytic colonies were transferred to plain broth, from the broth cultures blood agar plates made, and the single hemolytic colonies studied further. The hemolytic colonies on the plates were all of the beta type of hemolysis; that is, the hemolytic zone surrounding the colony was from 2 to 4 mm. in

* The complete paper will be found in The Journal of Infectious Diseases, 1919, Volume 25, p. 259.

diameter and the margin was sharp and distinct. Only those cocci were chosen for further study that grew into long chains in broth. A total of twenty-one strains was thus secured. Stock cultures were made on plain blood-agar slants. Typical hemolytic streptococci were isolated from the throat in 39 per cent. of thirty-two dogs examined.

Most of the hemolytic streptococci in the throat of the dogs studied were of the pyogenes type. Any close relationship could not be demonstrated between the groupings of the dog streptococci according to the results of fermentation tests and the results of test with antistreptococcus chicken serum.

January 13, 1919.

NATIONAL AND INTERNATIONAL RELATIONS OF SANITATION IN ECUADOR *

ARTHUR I. KENDALL
Chairman, Yellow Fever Commission

From the Patten Research Foundation, Northwestern University Medical School

Up to 1820, the vast majority of South American countries were under the subjugation of Spain. The United States has had in the past and will have in the future ever-increasing interest in these countries. The greatest menace that these countries offer to the United States and to the world at large is that which had to do with certain endemic diseases, and of these yellow fever and plague are the most formidable. Yellow fever at present is endemic on the west coast of Africa, Guatemala, certain parts of Mexico, and the west coast of South America, south of Panama to the northern border of Chile. In this region the disease prevails in areas of greater or lesser extent throughout the coastal plain, a distance of anywhere from twenty to forty miles, to the beginning of the Andean plateau.

* Read at joint meeting with Chicago Medical Society.

It is also endemic on the east coast of South America, in Colombia, Venezuela, and possibly in the great Amazon Valley of Brazil. Yellow fever, therefore, is largely an American disease and there are well authenticated histories of cases of yellow fever appearing as far north as New York and Philadelphia. In 1796 or thereabouts a rather extensive epidemic of yellow fever occurred in Philadelphia. Within the last few years New Orleans has suffered from yellow fever, and other southern cities at one time or another have been visited. Up to 1898 Havana, Cuba, enjoyed the somewhat doubtful honor of being called the pest hole of the American continent, and it was so regarded chiefly because of the prevalence of yellow fever there. Early in 1901 yellow fever disappeared, following the brilliant work of the medical corps of the American Army.

The mode of transmission of the disease was discovered by a commission headed by Major Walter Reed, and the practical measures suggested by General Gorgas (then Captain Gorgas) were put into effect. In October, 1906, the last case of yellow fever occurred on the Isthmus of Panama. As far as is known, there has never been a case since.

The great problem at present is to restrict the distribution of this disease until the time shall come when it will vanish from the face of the earth. Yellow fever is probably the easiest disease to conquer. The disease itself spreads only in warm weather. It is transmitted exclusively through the agency of a particular mosquito, which has enjoyed a large number of names since its discovery as the extrinsic host of yellow fever. The mosquito was originally known as the Culex fasciatus. When it was found that this insect was responsible for the transmission of yellow fever from man to man, a little more careful scrutiny revealed the fact that the mosquito did not belong to the genus Culex, and a new name, Stegomyia, was coined. Since that time the name has successively changed from Stegomyia fasciata to Stegomyia calopus and others.

The method of transmission of the organism of yellow fever appears to be very similar to that of Plasmodium malariae. The mode of transmission of malaria, with which practitioners are familiar, may serve as an illustration of the part the mosquito plays in the transmission of yellow fever.

There is a latent period between the time the mosquito bites an individual and the time when the mosquito becomes infective for another individual. This period is roughly from ten days to two weeks. So far as is known, a similar cycle in point of time takes place in the transmission of yellow fever. The female mosquito bites patients with yellow fever within the first three days of the clinical disease, and then a period elapses during which that mosquito is quite unable to transmit the disease to another, non-immune host. This period coincides quite accurately in point of time with the period elapsing between primary and secondary cases. There must be an extrinsic cycle in the mosquito which harbors the yellow fever organism quite as truly as there is an extrinsic period in the mosquito which harbors the malarial parasite. There is this difference between malaria and yellow fever, however. One attack of malaria by no means confers immunity or prevents infection. It predisposes to subsequent infection, or, more accurately, there is almost inevitably a series of relapses. It means that the individual infected with malaria may in successive intervals be a source of danger to other, non-infected individuals. Yellow fever is a disease which allows the host to recover from the infection and to remain immune for all time. At least, this is so in the great majority of cases. Furthermore, the disease may be transmitted only during a particular interval, this interval elapsing between the time of the original chill, which is quite common in yellow fever, and the period which is approximately seventy-two hours afterward. If this theory is correct, and the experimental evidence suggests it is, if every individual suffering from yellow fever should be screened and protected from mosquitoes at the time of the period just before the chill

until the period three or four days after the chill, yellow fever would cease to exist.

The methods of eradicating yellow fever are, first, to destroy the mosquitoes, which means the control of their breeding places, and also mosquitoes which are in the adult stage; secondly, to protect all febrile cases from the bites of mosquitoes during the three days or thereabouts in which persons are infective; and, finally, to be certain that non-immune individuals are kept out of unsafe areas. The method of exterminating mosquitoes is somewhat complicated in detail but simple in principle. It means careful drainage, inspection of all breeding places where the insects grow, and the destruction of adult mosquitoes by fumigation.

The problem in Havana and in Panama for the extinction of yellow fever was somewhat different from that in South American countries, and particularly in Ecuador, where the work is now going on. In Panama and Cuba the houses are, for the most part, of such construction that they can be fumigated quite readily, and one of the essential details of the elimination of yellow fever, as practiced in these places, was the careful fumigation of all of the houses at regular intervals in infected areas.

In Guayaquil, which is the principal point of infection at present, the structure of the houses is of such a nature as to render fumigation difficult. Earthquakes are common in Guayaquil; therefore, the construction of the buildings must be such as to safeguard the inhabitants from the danger of death by the collapse of buildings. The majority of the houses are made of frames which are joined in such a way that there is a certain amount of flexibility at the junction of the timbers, and these are covered with bamboo, which grows luxuriantly in the swamps in the lowlands of Ecuador, and is of fairly large size. It is obvious that such structures are by no means mosquito-proof, and fume-proof tents are placed over them during fumigation.

Success in exterminating yellow fever and mosquitoes depends particularly on conducting operations quietly to prevent the mosquitoes from flying around.

If unusual commotion is stirred up in placing these tents and putting them together, it will cause the mosquitoes to seek shelter elsewhere. There is great probability that these mosquitoes fly from place to place; hence, the question of fumigation is correspondingly complicated.

The mountaineers of Guayaquil are brought up in a country whose climate is much like our own. Yellow fever does not exist at the altitudes in which these mountaineers live; consequently, they are quite as susceptible to the disease as are persons from temperate zones. In the endemic areas the probability is that the children get yellow fever before they are many years old, and therefore the disease in the adults of the coastal plain region is practically unknown. People from the mountains, however, who come to the coast seeking employment or to embark for other countries and pass through Guayaquil or the coastal provinces, may become infected, and the influx of people from the highlands keeps yellow fever alive, in spite of the fact that the number of foreigners who visit Ecuador is small indeed.

Ecuador is handicapped, as are other countries in which yellow fever is endemic, in their commerce with the world. Ecuador is a wonderful country. It raises everything from the finest fruits of the tropics to those that are characteristic of temperate zones. It is near Panama and, since the Panama Canal is now open, many ships will require provisions and other products of Ecuador. Consequently, the elimination of yellow fever from Ecuador will give to that country a new life. If the country fails to rid itself of yellow fever, it will probably become bankrupt, and revolutions are almost certain to follow.

The International Health Board of the Rockefeller Foundation has charged itself with the duty of helping in international sanitation, and one of the groups in the International Health Board is the Yellow Fever Board, of which General Gorgas is chairman.

Some years ago General Gorgas and other yellow fever experts of this Board made a trip through the endemic areas of yellow fever in South America and

made known the prevalence of the disease there, and as a result of their trip and deliberations, it was decided that it is feasible and possible to eliminate yellow fever from the face of the globe. If this can be accomplished, and Ecuador can be freed from yellow fever, the United States will be regarded in an entirely different light than it is today by all Latin-American countries.

February 12, 1919.

CLINICAL AND PATHOLOGIC MANIFESTATIONS OF YELLOW FEVER

CHARLES A. ELLIOTT

Our clinical study was made in fifty consecutive cases of yellow fever. The histories elicited were fairly uniform. The first symptoms noted were a feeling of uneasiness, especially epigastric unrest, headache, backache, and aching of the extremities. Fever developed rapidly, often heralded by a chill or chilly sensations, which are frequently repeated. Nausea, and often vomiting, occurs repeatedly from the start, the latter usually bilious, although black vomit is noted by some of the patients as early as the second day. Fever, headache, backache, general muscular tenderness, and epigastric tenderness or pain, nausea and vomiting persist in various combinations until the admission of the patient to the hospital. A precipitous onset in uncomplicated cases, in which the patient gives a definite history of being well the day before the onset, is the rule.

In some patients who had been suffering from malaria for varying periods, a history of unusual symptoms, namely, sudden onset of nausea, vomiting, epigastric tenderness, headache, backache and persistent fever, was noted. This type of history of yellow fever developing during the course of malaria was present in four of thirty-nine cases in which reliable histories

* Read at joint meeting with Chicago Medical Society.

were obtained. In cases of this type the diagnosis was always uncertain until typical manifestations of yellow fever developed later, and most of these cases proved not to be yellow fever.

On admission the patient appeared restless and anxious, the face was flushed, the conjunctivae were injected, the gums were swollen, and they bled easily on pressure. Hemorrhages into the skin varying from 0.1 to several centimeters in diameter, usually irregular in outline, may occasionally be found on searching. Infected mosquito bites on the skin of the forearms or legs were frequently found. The mucous membrane of the mouth was congested. Herpes labialis was present in two cases. The lymphatic glands were not enlarged. The lungs were remarkable for being entirely free from findings except during terminal hypostasis and pulmonary edema. The cardiac findings were usually negative. Occasionally a precordial systolic murmur was heard during the height of the disease, and rarely extrasystoles were noted. The abdomen was usually tender throughout, the epigastrium and liver edge being exquisitely tender. The liver was not definitely enlarged except in a few cases. The spleen was definitely enlarged only in those suspected of being malaria; it was not palpable in most of the pure yellow fever cases. Tenderness on pressure over the flanks was usually marked. The skeletal muscles were usually tender on pressure throughout the course of the disease.

During the second period of the disease the patients were relaxed, usually quiet, and appeared dried out, jaundiced, weak, and apparently very ill, but otherwise the physical findings remained about constant. The fever was relatively low, continuous, and of short duration. It reached its height on the first day, continued remarkably constant for three or four days, and then gradually dropped to normal by the fifth to the eighth day. The pulse was apt to be relatively slow during the fever course, showing a marked dissociation between the pulse and temperature curves at that time, although early and late, after the temperature has reached normal, the pulse follows the temperature

curve. While a relative bradycardia of moderate degree is the rule, absolute bradycardia is unusual. A pulse of 50 or less was observed in only three of the series.

During the first few days of the disease the patient often complained of a sense of dyspnea, the only objective evidence of which was an occasional deep sighing respiration accompanied by a peculiar whistling expiratory note. Other than this, patients with light and moderately severe cases went through the entire course of the disease with apparently normal respirations. Jaundice was a constant, although variable manifestation in all cases. In general, it varied with the severity of the disease; in most light cases it was inconspicuous, although in some of these it appeared marked and out of proportion to the other manifestations of the disease.

The blood shows little that is characteristic. The white blood count averaged about normal, with a definite leukopenia of less than 4,000 in only nine cases.

The high counts, from 49,600 to 13,000, were obtained in moribund, usually uremic, patients; but it is noteworthy that some comatose patients gave normal white counts. The hemoglobin was universally low, but three estimations exceeded 90 per cent.; ten were between 80 and 90 per cent., and estimations between 40 and 60 per cent. were common. Nothing distinctive could be detected in the blood pressure determinations, except that it was uniformly low, systolic pressures of 110 or less, and diastolic pressures of 65 or less being the rule.

Hemorrhage constitutes one of the distinctive manifestations of yellow fever as seen in these cases. The principal structures which bleed are the nasal and gingival mucous membranes, and the gastro-intestinal and genito-urinary tracts. A history of early epistaxis was present on inquiry in seven cases. Extensive epistaxis occurred later, namely, on the fifth to the twelfth day in twelve cases. Melena was present in thirteen of thirty cases in which this point could be determined; and in three, large quantities of fresh blood were passed. In general, in all severe cases there was bleeding during the second and third week of the

disease, and in the light cases no bleeding at all. The administration of horse serum in six cases had no perceptible effect on hemorrhage. The urine of all yellow fever patients was extremely highly colored, varying from a dark yellow to olive green, the foam being always yellow. The amount passed varied from an average of 700 c.c. to complete anuria, which usually foretold death. Albumin began to appear as a trace on the second or third day, rapidly increased to enormous amounts, 3 or 4 gm. per liter during the second week, and then gradually decreased and finally entirely disappeared during the third or fourth week. In light cases, albumin and casts were present out of proportion to the other manifestations of the disease. Uremia occurred as a terminal condition in all fatal cases. The majority of the patients harbored intestinal parasites in the stools. Complications and sequelae were unusual. Parotitis occurred in two cases, phlebitis in one, and acute joint phenomena, such as pain and swelling of sudden onset, in three cases. Restitution progressed rapidly in all patients that recovered, although some were weak and many showed varying grades of jaundice at the time of discharge.

The greatest stress was placed on the following diagnostic points in the order named: 1. The fact that the patient was a foreigner and not a native of Guayaquil, or had recently arrived from the interior. The local physicians considered it practically impossible that a child born in Guayaquil should grow to maturity without having had yellow fever, and therefore was immune, and conversely, that a nonimmune adult could not live long in Guayaquil without having it. 2. A low, continuous fever course with relative bradycardia. A fever of 40 C. or over speaks against yellow fever. 3. Nausea and vomiting, black vomit being practically diagnostic. 4. Epigastric pain and tenderness, often intense from the first. 5. Rapid and progressive development of nephritis, albumin present as a trace on the second day, with from 1 to 3 gm. per liter on the fourth day. 6. Flushed and suffused face, injection of conjunctivae, and swollen and often bleeding gums. 7. The gradual and progressive develop-

ment of jaundice, a trace seen on the conjunctivae as early as the third day.

The greatest difficulty occurred when yellow fever developed in those already infected with malaria. In children with yellow fever, as seen in this series of cases, the manifestations were the same as those in the adults.

In relation to the prognosis, it was difficult to foretell the gravity of the case. Those admitted early with much facial congestion, injection of the conjunctivae and swollen gums, who were restless and apprehensive, and showed some dyspnea; were considered as having the disease in very grave form, and usually died. Tachycardia is always considered grave. All uremic phenomena, such as air hunger, restlessness, delirium and coma, accompanied by a lessening of the output of the urine to anuria, were grave signs, although not always fatal.

Of the fifty patients in this series, nineteen died, a mortality rate of 38 per cent., which was considered about the usual rate in Guayaquil. The mortality rate of yellow fever of all patients admitted to the lazaretto from Jan. 1 to Aug. 1, 1918, was 44 per cent.

Little treatment was attempted beyond the employment of general principles applicable in all fevers. Little or no medication was given, and no conclusions can be based on our experience in this regard.

Feb. 12, 1919.

AN ACQUIRED IMMUNITY TO AN ANIMAL PARASITE *

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The larval form of the commercial species of the fresh water mussel is an obligate parasite on definite species of fish for the completion of its metamorphosis.

* The complete article is published in The Journal of Infectious Diseases, Vol. 24, 1919, p. 337.

After two or three heavy infections of the parasite on the gills of the fish an absolute acquired immunity is developed in the host to any subsequent metamorphosis of the mussels.

The immunity is not due to a local increase of fibrous tissue nor to protective glands in the gills, but is a blood immunity of the host.

Serum from the immune fish has a cytolytic action on the glochidia (the larval form of the fresh water mussel). Whether a precipitin is present or not was not definitely determined.

March 10, 1919.

AN UNUSUAL CASE OF ANEURISM OF THE COELIAC AXIS AND ABSCESS OF THE BRAIN ARISING FROM A SEPTIC ENDOCARDITIS

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From the Laboratories of the City of Chicago Municipal Tuberculosis Sanitarium

Aneurisms of the coeliac axis and its branches are exceedingly rare. There are about forty-five cases of the former and a few more of the latter described in medical literature.

Out of the forty-five cases, one of the best described is that of Richardson[1] where the patient complained of severe pains in the gastric region, accompanied with nausea, vomiting and delirium. The patient also complained at times of a pulsating pain, arising in the region of the stomach. After palpation, this pulsation was found to come from a tumor in the region of the coeliac axis. Soon afterward this tumor ruptured and death followed. At the postmortem an aneurism of the coeliac axis was found. This same description would apply in general to most of the other cases.[2]

1. Richardson, B. W., Asclepiad, London, 1884, Vol. 1, pp. 97-113.
2. Lewis, T. C., Lancet, 1842-3, Vol. 1, p. 495; Irvine, J. P., Tr. Path. Soc. London, 1878, Vol. 29, pp. 85-90; Lyman, Boston Med. and Surg. Jour., 1879, Vol. 150, p. 309; Cleveland, J. L., Cincinnati, Lancet and Clinic, 1884; MS. 12, pp. 259-264; Lumsden, Dublin Jour. of Medical Sci., 1911, Vol. 130, p. 142.

The principal idea in giving it here is to contrast these cases with the one about to be described.

CASE REPORT

M. B., a poorly nourished girl of 12 years, was admitted to the Municipal Tuberculosis Sanitarium Dec. 19, 1917, to be held under observation for tuberculosis. She gave a history of diphtheria and scarlet fever followed by a protracted tonsillitis, within the previous sixteen months. On March 15, 1918, she developed a sudden temperature and upon examination, a double heart murmur was found and a diagnosis of endocarditis was established. One week later the patient was stricken with paralysis on the left side of the body, together with a sharp pain in the right frontal area of the brain. After a short coma she regained partial use of her left side, could hear but could not speak. April 28th, death occurred.

At necropsy the skin had a yellowish cast but would not ordinarily be called jaundice, the pupils were dilated and unequal, the right being much the larger. The lungs were normal, heart contained several cauliflower vegetations on mitral valve, a culture from which showed the causative organism to be streptococcus viridans. Mesenteric arteries and serosa were dark and injected with blood, mesenteric glands contained blood. Pancreas was firm and on microscopic examination showed considerable degeneration. The head of the pancreas contained a tumor about the size of a walnut. Upon removal this enlargement was found to be an aneurism at the branching of the coeliac axis, caused by a septic thrombus in the splenic artery. Part of the sac of the aneurism was filled with a laminated clot. Beneath this clot the gastric and hepatic arteries were found completely obliterated. The spleen was enlarged, dark red in color and congested. The liver apparently showed what Harley[3] described as acute biliary cirrhosis. There was a slight centralobular congestion, reddish in color, with a peripheral anemia having a yellowish color, and in which could be seen the dilated bile ducts. The brain was found to contain a large abscess in the corona radiata on the right side, containing the same organisms which were found in the heart valve. The internal carotid artery was found to contain a thrombus at the place where the middle cerebral artery was given off, similar to the one in the splenic artery.

3. Harley, British Med. Jour., 1898, Vol. 11, p. 1743.

Outside of the aneurism and its effects there is nothing very unusual in the case. This aneurism, occluding as it did the branches of the coeliac axis, completely obstructed the blood supply to the spleen and partially to the stomach, liver and pancreas; pressed down on the bile duct, superior mesenteric artery, abdominal aorta, portal vein, and completely occluded the main pancreatic duct. This condition was responsible for so many causes and effects it is difficult to enumerate them. It caused a backing up of the bile in the gall bladder and bile ducts, as well as an anemia of fresh blood to the liver and a reduced amount of portal blood. The latter was no doubt responsible for the hemorrhagic mesentery and mesentery glands. The function of the pancreas was greatly impaired, circulation to the lower extremities was greatly reduced by the pressure of the aneurism on the abdominal aorta, and as a result, blood pressure was increased in the coeliac axis, tending to cause an extension of the aneurism. The aneurism itself completely cut off the blood supply to the spleen and partially to the stomach, liver and pancreas. In fact, the inferior pancreatico-duodenal branch of the superior mesenteric, furnished the only blood supply to the pancreas, stomach and liver. This branch anastamoses with the superior pancreatico-duodenal branch of gastro-duodenal which is given off by the hepatic, far enough away from the aneurism in this case, to allow free passage of blood to the liver. Along the course of this anastomosis, branches are given off which supply the lower border of the pancreas, and the pyloric end of the stomach.

The condition in the brain, while interesting as a diverse complication, is in itself so classical that it needs no discussion in this brief report. The symptoms could all be accounted for by the location of the thrombus and from the symptoms the thrombus could be approximately located.

March 10, 1919.

PRIMARY CARCINOMA OF THE MAIN HEPATIC BILE DUCT

FRED H. STANGL

Primary carcinoma of the main hepatic bile duct is recorded by Humphrey D. Rolleston in twenty-two cases, accordng to data collected by him. In his descriptions the average age incidence is 56.5 years,

with 81 years and 29 years as the extremes. Males are affected three times as frequently as females. The association of this tumor with gallstones is unusual. Clinically the tumors are slow growing and death of the patient results before they are larger than an English walnut. Metastases occur late and then are not extensive. Infiltration into the liver adjacent to the tumor and involvement of the biliary and perigastric lymph glands usually is the extent of the secondary growth of the carcinoma. Symptoms, however, begin early, usually with pain and jaundice, both of which gradually become intense and constant.

In the present case the clinical record of the patient is as follows:

An Irish salesman, aged 76 years, entered the hospital on November 6, seeking relief from pain and soreness in the epigastrium, jaundice, dyspepsia, weakness and constipation. The onset of the symptoms was about three years previous to the admission date, and was associated with soreness in the epigastrium of gradual development. This was succeded by pain which was of a boring nature, constant in character and without any relation to food taking. Jaundice appeared a short time later and was first noticed in the sclerae. This slowly extended until the skin of the entire body was involved by an intense and constant yellow color. The dyspepsia complained of was chiefly a loss of appetite. Weakness and loss of weight were but minor symptoms except during the last few weeks previous to admission to the hospital.

Physical examination revealed a poorly nourished old white man with a marked generalized icterus. The chest was negative except for emphysema. There were no demonstrable changes in the heart. The abdomen was distended by gas. A tumor was visible in the epigastrium two inches to the right and below the xyphoid process. In the laboratory examination of the urine it was dark colored from the bile it contained but was free from albumen, sugar and casts. The stools were mushy in consistence, clay-colored and alkaline in reaction. Blood could not be demonstrated in the stools either macroscopically or chemically. The Ewald aspiration of the stomach contained no free hydrochloric acid with the dimethylamidoazobenzol indicator and N/10 sodium hydrate as the titrating agent. The total acidity of the test meal was 18 points in the tenth normal sodium hydrate titration. Blood could not be demonstrated in the

gastric contents. The roentgenological department made a diagnosis of a malignant lesion involving the pylorus of the stomach. Blood examination revealed 77 per cent. hemaglobin (Sahli); 3,480,000 red blood cells and 16,400 white blood cells. Rectal temperature ranged from 98 to 100.6 degrees F. The pulse rate varied from 70 to 88 per minute and the respirations were between 20 and 24 per minute. The clinical diagnosis made at that time was: Carcinoma of the stomach, liver metastasis, obstructive jaundice.

Seven days after admission the patient became stuporous and had involuntary passages of urine and feces and four days later, eleven days after admission, he died.

Postmortem examination of the patient was made the same day. A small walnut-sized, firm, white carcinoma was found arising from and occluding the main hepatic bile duct and lying entirely within the liver parenchyma. The extrahepatic bile ducts were unchanged. The carcinoma had infiltrated the adjacent liver tissue for a depth of 1.5 cm. and secondary carcinomatous nodules were also demonstrable in the biliary lymph glands. Small pea-sized gallstones, about eight in all, were present in the intrahepatic bile ducts, in the gallbladder and in the ampulla of Vater. The intrahepatic bile ducts were markedly distended with mucoid bile. The mucous and serous surfaces, as well as the skin and sclerae, were deeply bile stained. The stomach was unchanged except for a few fibrous adhesions between the pylorus and the fundus of the gallbladder.

Microscopic examination revealed an infiltration of carcinoma cells in glandular arrangement arising from the lining of and entirely occluding the intrahepatic portion of the hepatic bile duct. Carcinoma tissue similar to this was present in the adjacent liver parenchyma and in the biliary lymph glands.

March 10, 1919.

A CASE OF SPONTANEOUS RUPTURE OF THE ESOPHAGUS

RICHARD W. WATKINS

From the Pathological Laboratory of Rush Medical College

Spontaneous rupture of the esophagus is rare. Brosch has recorded eight cases in a review of the literature since 1724. One case has come under my observation in Dr. Le Count's laboratory.

A machinist, 49 years old, was brought to the Cook County Hospital one afternoon at 4:30, complaining of pain in the upper left quadrant of his abdomen, nausea and vomiting and dyspnea of two days' duration. Examination showed an absence of the right eye (due to an old injury), crepitation of the skin and subcutaneous tissue at the base of the neck, a leukocyte count of 10,200, an irregular pulse with a rate of 128.

He was prepared for an abdominal operation when death occurred, eight hours after his entrance to the hospital.

Postmortem examination revealed a rupture of the esophagus into the left pleural cavity, bilateral pneumothorax, compressed left lung, food in the left pleural cavity, bilateral emphysema of the subcutaneous tissue of the neck, slight bilateral fibrinous pleuritis, and marked syphilis of the aorta.

Examining the region about the perforation the following condition was found: A smooth and shiny mucosa of the esophagus red in its upper portion from the blood in the underlying vessels, spotted with epithelioses which are more numerous in the upper third than in the lower two thirds. Through the length of the esophagus this layer is thrown into longitudinal folds. In the posterior wall at the junction of the esophagus and the stomach is a longitudinal perforation, 7 cm. long and 1 cm. wide in its widest portion. Near its border the mucosa is red from blood in the underlying blood vessels. The wall here is no thicker than that further out and is of the same soft consistency. Near the middle of the perforation it is crossed by the wavy line marking the transition of the epithelium of the esophagus to that of the stomach. The mucosa of the stomach is brown and velvety and has a few petechial hemorrhages in it. The pouch of the stomach contains partly digested food, meat and beans being recognizable.

The dorsal mediastinum is thick and soft and covered on the right and left sides with pleura. That on the right is thick and fibrous with air bubbles lifting it from the underlying tissue. On the left the pleura is thick and fibrous posteriorly, but this merges into a thin mesh of fibrous tissue anteriorly where there are two distinct apertures near the junction of the upper two thirds with the lower third. The more superior aperture is 2.5 cm. long and the other 1.5. Through these thick brown mucus and partly digested food can be pressed out. On opening this part of the mediastinum it is found to be distended and a large cavity formed between its walls. This extends from the under surface of the arch of the aorta to the diaphragm, and is traversed through its length by thick fibrous strands with the spaces

between packed with food and mucus. Probing into the aperture in the wall of the esophagus it is found to open into the dissected cavity in the mediastinum. The lymph glands of the mediastinum are black but not enlarged. In the intima of the aorta are tough yellow thickenings, especially thick about the arch of the aorta where they almost completely line the vessel.

Microscopically the layers of the wall of the esophagus appear frayed out along the border of the perforation and the broken edges are irregular and covered with fibrin. The epithelium of the mucosa is lacking in the section. In the reticulum of connective tissue between the circular muscle bundles are a few fibroblasts and many closely packed polymorphonuclear leukocytes. The longitudinal muscle bundles are more compact but between these two are polymorphs. Clumps of these cells occur in the subserous connective tissue.

The cause for the perforation is obscure. There is no cirrhosis in the liver to account for the distention or rupture of esophageal veins and no scars are found in the mucosa, nor induration to indicate a chronic process.

March 10, 1919.

TRANSPLANTATION OF PERIPHERAL NERVES *

G. CARL HUBER

The data to be presented have been gathered in the course of experimental work carried on in conjunction with the Division of Head Surgery of the office of the Surgeon General and extend over a period of somewhat more than one year. During this period Lieut.-Col. Dean Lewis, Major J. F. Corbett, Major Byron Stookey and Capt. Theodore Roberg have in succession received assignment to the Department of Anatomy, University of Michigan, where this work has been carried on. To their initiative and untiring and hearty cooperation, the progress of the work and the results obtained owe much.

In the prosecution of the experimental operative work strict asepsis was followed. So far as possible

* Read at a joint meeting with the Chicago Neurological Society.

the surgical technic was that of modern aseptic surgery. In practically all of the experimental operations union was by primary intention.

Owing to the difficulty of obtaining catgut sutures of suitable size and quality for uniting resected nerves, we were early in our work led to adopt a silk suture and as technic developed, Triple O, Corticelli silk thread, unraveled so as to obtain three fine threads, became the standard suture in nerve repair. Before use the sterilized threads were thoroughly waxed with sterile wax, this facilitating greatly the application of the suture. In practically all of our experiments of nerve transplantation the silk suture was passed through the nerve trunk and nerve transplant. The passing of a silk suture through a nerve trunk and transplant is innocuous, the silk suture becoming early encapsulated in a thin layer of connective tissue which does not materially interfere with the down growth of central neuraxes.

The tissues obtained from the animals operated on have for the greater part been stained after the pyridine-silver method, and for many of the experiments were sectioned at close intervals, in cross and longitudinal sections, for the length of the nerve operated on. This method gives a differential staining for the neuraxes, especially desirable in a study of the regenerative processes of peripheral nerves.

Regarding nerve regeneration, we maintain that regeneration of a degenerated portion of a peripheral nerve is through downgrowth of new neuraxes derived from the central nondegenerated portion of said nerve, the peripheral degenerated portion taking no immediate part in the regeneration of the neuraxes.

In the earlier stages of this experimental work and in association with Lieut.-Col. Dean Lewis, the question of injecting absolute alcohol into a living nerve, and related problems, was dealt with in four series of experimental observations. Though not coming immediately within the question under consideration, they have a bearing on certain of the experiments to be considered. In one of these series the use of absolute alcohol to obviate the formation of amputation neuroma

was tested. Series No. 1: Sciatic of rabbits: thirty-three experiments; respective animals under observation for periods varying from two days to 157 days. The sciatic of rabbits was exposed and injected in about the middle of the leg with about 0.5 c.c. of absolute alcohol, in two or three point injections. The sciatic was then cut 3 mm. to 5 mm. distal to the point of injection and 1 cm. to 1.5 cm. of the distal sciatic stump resected. The wound was then closed. The operated animals were killed at intervals and it was observed that this simple procedure obviated the formation of amputation neuroma. In a control series (Series No. 2), it was ascertained that amputation neuromas form after every section of a peripheral nerve, even though the section be made under strict asepsis, with immediate closure of the wound and with wound healing by primary intention. In central nerve stumps injected with absolute alcohol, exposed and examined at stated intervals, it was noted that such central stumps terminate in a fine tapering end with no appreciable enlargement. Four to five weeks after section and alcohol injection, fine, newly formed neuraxes penetrate these tapering ends and may even grow beyond, but these downgrowing neuraxes do not present the tangle and excessive proliferation of new nerve fibers noted in an amputation neuroma, and there is primarily no proliferation of sheath cells. For use in human surgery it is recommended that 1 c.c. to 2 c.c. of absolute alcohol be injected into the distal end of the nerve stump, 1 to 2 cm. central to the cut end of the nerve. It is suggested, especially for the larger nerves, that a series of point injections be made, perhaps in two or three tiers, so that all parts of the nerve be reached with absolute alcohol. This method can be recommended as a simple and efficient method for preventing the formation of amputation neuroma.

In a further series (Series Nos. 3 and 4) the behavior of a living nerve injected in course with absolute alcohol or acetone, and without cutting the nerve, was experimentally studied. The injection of absolute alcohol into a living nerve causes fragmentation of the neuraxes and myelin in the field coming

under the immediate influence of the absolute alcohol. This fragmentation differs from that of Wallerian degeneration and is not accompanied by a primary proliferation of sheath cells. In due time regeneration by the downgrowth of central neuraxes follows. In cases of severe neuralgia, in which section of the nerve is contemplated, injection of absolute alcohol without nerve section should be considered.

The great majority of our experiments have dealt with the question of bridging nerve defects of such extent that the severed nerve ends, after the necessary repair and resection, cannot be brought end to end, without undue tension, by process of simple suture. In this connection the question more immediately under discussion, namely, nerve transplantation, received especial consideration. In the series of experiments listed, the following nomenclature was used: A segment of nerve used to bridge a defect in a peripheral nerve, taken from another nerve of the same individual, is designated an auto-nerve-transplant; a segment of nerve taken from another individual, but of the same species, is designated a homo-nerve-transplant; a segment of nerve taken from another individual and of a different species is designated a hetero-nerve-transplant. Collateral questions, such as the use of certain membranous structures for purposes of sheathing a nerve transplant and suture lines; the question of the use of tubular sutures in nerve repair and of nerve suture under undue tension, subjected to experimental test are not reported on at this time.

Experimental observations warrant the conclusion that bridging nerve defects by means of nerve transplants is a legitimate operation and one to be recommended in cases where there is loss of nerve substance of such extent that ordinary suture cannot be made without undue tension. The experimental observations dealing with nerve transplantation and related questions are here considered under the following series:

Series No. 5. *Auto-nerve-transplants.*—Sciatic of dogs: seventeen experiments, with respective animals under observation for periods varying from eleven days to 382 days.

In these experiments the sciatic nerve was exposed and resected to the extent of 2.5 cm. to 3 cm. The resultant defect was bridged by means of a segment or several segments of nerve taken from one of the sensory cutaneous branches of the same dog. In our experiments the transplant was taken from the cutaneous radial branch. Since in surgical practice in dealing with the repair of the larger nerves, the resection of a normal nerve of approximately the same size for purposes of obtaining an auto-nerve-transplant is not justified, it has been the procedure to use for an auto-nerve-transplant a segment of one of the cutaneous nerves of much smaller size than the nerve to be bridged. The resultant difference in the size of the nerve to be bridged and the transplant has mitigated against obtaining optimum results. It occurred to us that this difference in size of transplant and nerve to be bridged might in a measure be overcome by making use of several segments of a smaller nerve to bridge the defect in a larger nerve. This procedure we designate a "cable-auto-nerve-transplant." In eight experiments out of the seventeen of this series this method was tested by taking four segments of the cutaneous radial nerves to bridge a defect in the sciatic. These segments were sutured separately or in groups of two, both centrally and distally, between the resected ends of the sciatic. In the remaining nine experiments of the series the defect in the resected sciatic was bridged by using, respectively, one segment of the cutaneous radial, five experiments; two segments, three experiments; three segments, one experiment.

The observations made on these experiments may be summarized by stating that the cable-auto-nerve-transplant presents a method for bridging nerve defects which gives every promse of favorable result. Within a few days after the operation the several segments of nerve transplanted become surrounded by connective tissue, so as to form an apineural sheath, binding them together in one nerve trunk in which the funicular arrangement of the several nerve segments transplanted is fully maintained. Downgrowing neuraxes coming from the central stump penetrate and pass

through the several funiculi to reach the distal segment which in time becomes penetrated by new neuraxes. These experiments have been carried on for a time of sufficient length to obtain new motor nerve endings in the calf and planter muscles and evidence of sensory regeneration. It is admitted that this operation is tedious, requires care and some skill and necessitates the making of a second wound. However, the experimental results justify its recommendation. In surgical practice the cutaneous radial and the cutaneous portion of the musculo-cutaneous of the arm, the lesser sciatic, and especially the sural of the leg may at convenience be selected as the nerves from which segments for a cable-auto-nerve-transplant may be taken.

Series No. 6. *Homo-nerve-transplants.*—Sciatic of rabbits: seven experiments, with respective animals under observation for periods varying from eight days to eighty-three days.

In these experiments a segment from the sciatic of one rabbit was used to bridge a defect in the sciatic of another rabbit experimentally resected. These experiments show that a fresh homo-nerve-transplant may be employed to bridge a nerve defect with every promise of success. Since chance alone would permit this operation in surgical practice, other experiments dealing with homo-nerve-transplants were devised and will be considered in this report.

Series No. 7. *Hetero-nerve-transplants.*—Sciatic of rabbits: thirty-nine experiments. In sixteen of these the two sciatics of half-grown guinea-pigs were used to bridge a defect in the sciatic of grown rabbits; in twenty experiments one of the sciatics of a full-grown guinea-pig was used to bridge a defect in the sciatic of a full-grown rabbit; in three experiments one of the major nerves of a dog was transplanted to a sciatic of a rabbit. The respective animals were under observation for periods varying from three to over 300 days.

The question of the possibility of using hetero-nerve-transplants is of academic and practical interest. The ease with which fresh, normal nerves may be obtained

as hetero-nerve-transplants warrants the interest taken by surgeons in experiments dealing with hetero-nerve-transplants. Opinions current in literature are not unanimous as concerns experimental observations on hetero-nerve-transplantation. Our own results may be summarized in this brief abstract in the statement that neurotization of the distal stump through a hetero-nerve-transplant is experimentally possible. However, the results obtainable are not as certain and not as favorable as when auto- or homo-nerve-transplants are used, and the resultant distal regeneration not as complete. Therefore, this procedure cannot be recommended as an operation of choice in surgical practice.

The following series of experiments deals with the use of degenerated auto-, homo- and hetero-nerve-transplants. Every nerve transplanted undergoes degeneration. It seemed worthy of experimental test as to whether nerves degenerated before transplantation would prove more favorable for downgrowth or central neuraxes than nerve transplants taken from fresh, normal nerves which would undergo degeneration after transplantation.

Series No. 8. *Degenerated Auto-nerve-transplants.* —Sciatic of dogs: three experiments; respective animals under observation for periods varying from 127 to 416 days.

In this series of experiments the sciatic nerve was cut and the wound closed. About twenty days later the cut sciatic was again exposed and a segment of the degenerated distal stump transplanted to the resected ulnar of the same dog. The experiments of this series are too few to warrant drawing definite conclusions. The statement seems justified that regeneration of the distal stump of a resected nerve through a degenerated auto-nerve-transplant is possible, but that such regeneration is not more favorable nor more rapid than when a nondegenerated auto-nerve-transplant is used.

Series No. 9. *Degenerated Homo-nerve-transplants.* —Sciatic of dogs: five experiments; respective animals under observation for periods varying from seventeen days to 328 days.

For this series the sciatic nerve of a number of dogs was cut and wound closed. Some twenty to thirty days later the cut sciatic was again exposed and a segment taken from the degenerated distal stump and transplanted to bridge a defect in a resected sciatic of another dog. The observations made on these experiments warrant the general conclusion that regeneration of the distal stump of a resected nerve may be obtained through a degenerated homo-nerve-transplant. The possibility of using a degenerated nerve as a homo-nerve-transplant in surgical practice is warranted by these observations.

Series No. 10. *Degenerated Hetero-nerve-transplants.*—Sciatic of rabbits: eighteen experiments; respective animals under observation for periods varying from three to 244 days.

For these experiments one of the major peripheral nerves of a dog was cut and allowed to degenerate for periods varying in the respective experiments from about twenty days to thirty days. A segment of the degenerated nerve was then transplanted to the resected sciatic of a rabbit. The syncytial, nucleated strands found within the sheaths of degenerated peripheral nerves, having undergone Wallerian degeneration, may be regarded as simulating embryonic tissue. Such tissue, it was argued, should prove more favorable for downgrowth of central neuraxes than would be the nondegenerated nerve fibers of a hetero-nerve-transplant. The observations made on this series of experiments do not bear out this assumption. It was observed that the degenerated hetero-nerve-transplant undergoes a secondary degeneration. In certain of the experiments downgrowth of the central neuraxes through and on the degenerated hetero-nerve-transplant was obtained. However, the results, even in the experimental observations, were so uncertain that the adoption of this procedure in surgical practice is not warranted.

The following series of experiments was devised to test the possibility of storing homo-nerve-transplants for a period of several weeks before use. The possi-

bility of obtaining human nerves under aseptic precaution, from amputated limbs, and storing them until operative procedure demands their use, would obviate the difficulty experienced in surgical practice of obtaining fresh human nerves on demand.

Series No. 11. *Homo-nerve-transplants Stored in Vaselin.*—Sciatic of rabbits: eight experiments; respective animals under observation from periods varying from sixty-six days to 155 days.

Dujarier and Francois[1] in a series of twenty-four cases reported the use of homo-nerve-transplants stored in vaselin before use in operative procedure. They recommend that the nerves be removed from amputation stumps under aseptic precautions, be placed at once into warmed, sterile vaselin, and then kept at nearly 0 C. temperature. Nerves were thus kept for several weeks. Before use the vaselin was again warmed, the nerve removed and washed in warm sterile serum. Twenty-four cases were operated on and reported before sufficient time had elapsed to enable determining the ultimate results. It is reported that in all cases but one the healing of the wound was by primary intention.

At the time our experiments were undertaken we were unable to find any experimental observations on this method. In our experiments the method suggested by the French observers was followed as closely as the brief account descriptive of the method permitted. The sciatics of full-grown rabbits were removed under asepsis, placed at once into sterile vaselin, contained in tubes warmed to the melting point of the vaselin. The tubes were then placed in a small ice chest at constant temperature of 3 C. In the several experiments, after periods varying from four to thirteen days, the nerves thus treated were used to bridge defects of about 3 cm. length caused by resection of the sciatics of rabbits. The results of these experiments are gratifying. Functional return was noted in the experiments of longer duration. Time has not permitted a histologic study of the tissue removed. In the experiments

1. Bull. at Mem. Soc. Chir., Paris, 44, Jan. 1918.

of shorter duration a microscopic study of the transplant shows abundant downgrowth of central neuraxes through the transplant. The experimental observations warrant the statement that this method, as suggested by the French observers, deserves consideration in surgical practice.

Series No. 12. *Homo-nerve-transplants Stored in Liquid Petrolatum.*—Sciatic of rabbits: Forty experiments; respective animals under observation for periods varying from one hour to 229 days. (To date certain of the animals are still under observation.)

Under the method of storing nerves in vaselin (Series No. 11), it is necessary to warm the vaselin to the melting point before the nerve segment can be placed therein, likewise when the nerve segments are removed therefrom. To obtain sterile serum is not always easy. For these reasons we have devised a simple method which consists in storing nerves in liquid petrolatum. We have used Squibb's Liquid Petrolatum. This is a clear, bland fluid. The required quantity was placed in large tube vials, corked with cotton plugs, then autoclaved on successive days. After cooling to room temperature the tubes with liquid petrolatum were placed in the ice chest and cooled to 3 C. The sciatics of full-grown rabbits were removed with asepsis, placed in the cooled and sterile liquid petrolatum and kept at 3 C. Nerve segments thus stored in liquid petrolatum were used in the several experiments after storage of from four to thirty-nine days, as nerve transplants to bridge defects of approximately 3 cm. in length in the sciatic of rabbits. For each experiment the tube containing the nerve transplant was taken from the ice chest just before the operation, and when required, the nerve transplant was taken from the liquid petrolatum, and this allowed to drain off by holding the nerve segment suspended from one end by means of forceps. Sutures were then placed near each end of the nerve segment and the ends cut by means of sharp scissors to within about 2 mm. of the sutures. The nerve segment was then sutured to the two ends of the resected sciatic. Nerves stored in this manner, even for a period of thirty-nine

days, retain their color and consistency remarkably well. The experimental animals of this series of longer duration, six months or over, have not as yet been killed and examined. The experiments completed and fully studied warrant the conclusion that neuraxes derived from the central end will grow through a homo-nerve-transplant having a length of 3.5 cm. and stored in liquid petrolatum for a period of somewhat over five weeks quite as well as through a freshly removed homo-nerve-transplant. Very satisfactory neurotization of the degenerated distal segment has been obtained through a homo-nerve-transplant stored in liquid petrolatum, having a length of somewhat over 3 cm., 100 days after the operation. Experimental observations warrant the statement that the use of human nerves obtained from amputated members and stored in liquid petrolatum as here directed for the purpose of bridging nerve defects deserves serious consideration as a surgical procedure.

Series No. 13. *Homo-nerve-transplants Stored in Sterile 50 Per Cent. Alcohol.*—Sciatic of rabbits: eighteen experiments, with respective animals under observation for periods varying from two days to 151 days. (Certain of the animals of this series are still under observation.)

Nageotte[2] has recommended the use of nerve transplants stored in 50 per cent. alcohol. For this series the sciatics of full-grown rabbits were removed under asepsis and placed at once into 50 per cent. alcohol contained in wide-mouth, glass-stoppered bottles. In the 50 per cent. alcohol the nerve segments were stored for periods varying in the several experiments from seven days to twenty-nine days. Just before use as a nerve transplant the nerve segment was taken from the 50 per cent. alcohol and placed in a dish containing sterile salt solution in which they remained fifteen to twenty minutes. When taken from the 50 per cent. alcohol the nerve segments are quite hard, though not brittle. After a short stay in the normal salt solution they again become quite pliable. The nerve segments

2. Bull. et Mem. Soc. Chir., Paris, 44, 1918.

were taken from the normal salt, sutures placed, the ends freshened by cutting with sharp scissors about 2 mm. from the suture lines and the operation completed by transplanting the nerve segment into a defect caused by resection of the sciatic of a rabbit. Time has not permitted conclusive observations on this series. The observations made thus far indicate clearly that downgrowing neuraxes coming from the central stump penetrate readily a homo-nerve-transplant having a length of 3 cm. and stored in 50 per cent. alcohol for nearly four weeks, and thus guide the downgrowing neuraxes to the degenerated distal stump.

In this series of experiments of homo-nerve-transplants stored in vaselin, liquid petrolatum, or 50 per cent. alcohol, the observations indicate that the nerve segments thus stored do not retain a latent viability. The sheath cells of the transplants show no evidence of proliferation and appear not to have a biologic significance. The neurolemma sheaths of the transplanted nerve fibers are well preserved and through these the downgrowing neuraxes of the central stump find ready paths and thus reach the distal stump. Therefore, it seemed desirable to test the behavior and the value of hetero-nerve-transplants stored in liquid petrolatum and 50 per cent. alcohol, and for this purpose the following series of experiments were undertaken.

Series No. 14. *Hetero-nerve-transplants Stored in Liquid Petrolatum.*—Sciatic of rabbits: six experiments; respective animals under observation for periods varying from five to 117 days. (Certain of the animals of this series are still under observation.)

For this series certain of the major nerves removed from dogs under strict asepsis were stored in liquid petrolatum, as described under Series No. 12, for periods varying from eleven days to twenty-five days, and then used as nerve transplants to bridge defects in the sciatic of rabbits caused by resection. None of the longer time experiments of this series have thus far been studied histologically. Therefore, no conclusions as to the value of this method can at the present time be drawn.

Series No. 15. *Hetero-nerve-transplants Stored in 50 Per Cent. Alcohol.*—Sciatic of rabbits: three experiments; respective animals under observation for periods varying from sixty-four days to 117 days. (Two of the animals are still under observation.)

For this series certain of the major nerves of dogs were removed and stored in 50 per cent. alcohol, as described in Series No. 13. They were then used to bridge defects in the sciatic of rabbits. Two of the animals of this series are still under observation; the other experiment was terminated by death of the animal too soon after operation to admit of drawing definite conclusions.

References are frequently made in surgical literature to the use of certain membranous structures employed as sheaths which are wrapped about nerve transplants or suture lines. Concerning the necessity or value of such sheaths there is no unanimity of opinion. The following series of experiments was undertaken to test their value. It should be stated that it is here recognized that the clean, surgically aseptic, operative wounds in animal experiments, made through normal tissue, do not simulate the operative wound in surgical practice in many cases of secondary nerve suture, made in the presence of abundance of cicatricial tissue. However, it was hoped that certain general principles might be ascertained to serve as guides in surgical practice.

Series No. 16. *Auto-nerve-transplant with Nerve Transplant and the Suture Lines Wrapped in Several Layers of Cargile Membrane.*—Sciatic of dogs: thirteen experiments, with respective animals under observation for periods varying from twenty hours to 359 days.

In these experiments we made use of Cargile membrane prepared by Johnson & Johnson. The left sciatic and the right ulnar nerves of respective dogs were exposed and a segment of the right ulnar 3 to 4 cm. long was transplanted to bridge a defect in the sciatic caused by resection. After suturing the transplanted ulnar, the transplant and the sutures were surrounded by two or three layers of Cargile membrane, closely

applied and wrapped about this nerve. The wound was then closed. Untreated Cargile membrane, as here used, it was found, was absorbed within a period of ten days; that is to say, before it could serve a purpose in preventing connective tissue formation in the immediate vicinity of the transplant and suture lines. Therefore, its value in surgical practice is seriously questioned.

The difficulty of obtaining Cargile membrane at the time these experiments were made led us to attempt resterilization of that portion of each membrane not used at any one operation. This was accomplished by placing the same in 70 per cent. alcohol in which they were stored, often for days. Before their use they were placed several hours in absolute alcohol and before use in operations taken from the absolute alcohol, spread out on dry sterile towels and allowed to dry. In five of the thirteen experiments of this series such alcoholized Cargile membranes were used to wrap the nerve transplant. It was found that this very simple method very materially alters the absorbability of the Cargile membrane as found in the market. In one experiment terminated nearly five months after the operation distinct evidence of the Cargile membrane was found. In another experiment terminated nearly seven weeks after the operation the alcoholized Cargile membrane was found to have been practically unaltered and remained closely wrapped about the nerve. There was evident no material increase of connective tissue about the alcoholized Cargile membrane thus used as a sheath.

The use of alcoholized Cargile membrane, prepared as above stated, in double or triple layers, as a sheath for wrapping nerve transplant or suture lines after nerve suture, when such sheathing is deemed necessary, deserves consideration in surgical practice.

Series No. 17. *Auto-nerve-transplant Wrapped in Autofascial Sheath.*—Sciatic of dogs: fifteen experiments, with respective animals under observation for periods varying from fourteen days to 324 days.

In this series of experiments the left sciatic and right ulnar, or vice versa, were exposed and a segment of

the ulnar transplanted to the sciatic. After suturing the transplant in place this was wrapped in a piece of fascia lata taken from the same dog. The fascial membrane taken was removed and trimmed to such size that when applied it extended about 8 mm. beyond the central and distal suture lines of the transplant, and when wrapped about the nerve formed a closely fitting tube with edges overlapping about 5 mm. Fine silk sutures and several half mattress sutures were placed to hold the sheath in position and complete the tube. The experiments of this series admit the general conclusion that an autofascial sheath is very slowly absorbed, evidence of its persistence having been observed three months after operation. However, even in the aseptic wounds made in normal tissue, where use could be made of the fascial planes for exposing the nerves, there is observed a distinct connective tissue proliferation about the fascial sheath, to such extent as to prejudice against this procedure in surgical practice, especially in operations where nerve repair is made through and in cicatricial tissue.

Series No. 18. *Auto-nerve-transplant with Nerve Wrapped in a Formalized Arterial Sheath.*—Sciatic of dogs: eight experiments; with respective animals under observation for periods varying from six days to 241 days.

In this series of experiments the left sciatic and right ulnar, or vice versa, were exposed and a segment of the ulnar transplanted to bridge a defect in the resected sciatic. After the transplant was sutured in place, this was surrounded by a sheath prepared from the wall of a formalized artery. The carotid arteries of large dogs were removed and stretched over glass rods of suitable size. They were then fixed in 5 per cent. formalin for forty-eight hours; washed in water twenty-four hours; boiled in distilled water for twenty minutes; then stored in 70 per cent. alcohol in sterile, wide-mouth, glass stoppered bottles for several days to several weeks, as necessity demanded. Before use, a segment of the fixed artery of required length was slipped from the glass rod, cut longitudinally along one side and placed in sterile normal salt solution for about

thirty minutes. The arterial sheath thus prepared was then wrapped about the nerve transplant and allowed to extend over the suture lines about 5 mm. and fixed in place by central and distal stay sutures and several half mattress sutures, using fine silk. The experiments of this series admit of drawing the following general conclusions: that a formalized arterial sheath, prepared as above stated, remains in place and without absorption for several months and this without inciting material increase of connective tissue. It is more particularly the elastic tissue of the vessel wall that resist absorption. Since formalized arterial sheaths are easily prepared and may be kept on hand in sterile condition in 70 per cent. alcohol, and are easily applied, this method deserves consideration in surgical practice, when sheathing of a transplant or suture line in nerve repair is deemed desirable.

Series No. 19. *Auto-nerve-transplant with Completely Detached Auto-fat Sheath.*—Sciatic of dogs: two experiments; animals under observation, one, 4 days; the other, 324 days.

In this series the left sciatic and right ulnar were exposed and a segment of the ulnar transplanted to the sciatic. The nerve transplanted and the suture lines were then wrapped in a membrane of subcutaneous fat, taken from the same animal to one side of the sciatic wound. After removing the membrane of fat, which had an average thickness of about 5 mm., this was gently washed in sterile normal salt solution, so as to remove as far as possible the adherent blood, and was then wrapped about the nerve transplant and suture lines. The sheath was held in place by the use of several fine silk stay sutures. One of these experiments was terminated by the death of the animal four days after operation; in the other the animal was killed 324 days after operation. In this latter experiment, regeneration of the distal segment was obtained. However, the region of the transplant was surrounded by a distinct layer of dense fibrous tissue occupying the region of the fat sheath and binding the transplant to the subcutaneous tissue. Definite conclusions based

on this single experiment seem hardly warranted. However, the result obtained argues against the use of a completely detached sheath, even when this is taken from the same animal, since the fat membrane is replaced by dense fibrous tissue.

Series No. 20. *Tubular Suture by Use of Formalized Artery.*—Ulnar nerve of dogs: twelve experiments; respective animals under observation for periods varying from 4 days to 298 days.

In this series we made use of the resected ulnars of certain of the experiments in Series Nos. 16 to 19, to test experimentally the value of an arterial tubular suture as recommended by Foramitti and since used in the Russo-Japanese War by Hashimoto. The formalized arterial tubes were prepared as stated under Series No. 18, essentially as described by Foramitti. Before use the formalized carotid artery of a large dog was taken from the glass rod and a segment about 1 cm. longer than the defect in the nerve to be repaired was removed and placed for about one-half hour in sterile normal salt solution. A fine silk suture armed with a fine needle at each end was then passed through the central and distal stump of the resected ulnar about 2 to 3 mm. from the respective ends of the tube and the ends of the resected nerve, central and distal, drawn into the lumen of the arterial tube and held in place by knotting the silk sutures over one side of the arterial tube. The wound was then closed by using the necessary facial and skin sutures. In this series of experiments no nerve-transplant was inserted, the ends of the resected ulnar, 4 to 5 cm. apart, were merely inserted into the ends of the arterial tube and kept in place by means of stay sutures.

In this series, as stated for series No. 18, it was found that the formalized artery resists absorption for a period of at least three months. In certain of the experiments it was evident that one or the other of the ends of the nerve had been pulled out of the lumen of the arterial tube, sometime soon after the completion of the operation. In two of the experiments of more than three months' duration neurotiza-

tion of the distal ulnar was obtained through downgrowing neuraxes of the central stump, conveyed to the distal stump through the lumen of the formalized artery. This series confirms the possibility of obtaining regeneration of the distal degenerated end of a nerve, after loss of 4 to 5 cm., through a tubular suture in case the tubular suture resists absorption for a period of sufficient length to admit of downgrowth of the central neuraxes to the extent of reaching the central end of the degenerated distal stump. However, the method cannot be recommended for adoption in surgical practice since other methods for bridging nerve defects offer greater assurance of success.

Series No. 21. *Direct Suture of Nerves Under Tension.*—Ulnar nerve of dogs: eleven experiments; respective animals under observation for periods varying from twenty-two to 324 days.

In this series use was made of the resected ulnar nerves of certain of the experiments in Series Nos. 16 to 19. A silk suture was passed through the central and distal stumps of the ulnar resected to the extent of 4 to 5 cm. and by applying tension and flexing the limb the resected nerve ends were brought to as close approximation as possible and sutured. In a number of these experiments the line of suture was wrapped with several layers of alcoholized Cargile membrane or a formalized artery sheath was applied. In other experiments the wound was closed without sheathing the suture line. Purposely, no endeavor was made to immobilize the limb. On opening the wounds in the several experiments at stated intervals, it was noted that in all but one experiment the suture had torn out either centrally or distally and that the nerve ends had separated for a distance about equal to that obtained before the tension sutures were applied. In the one experiment in which the suture did not appear to have been torn out, limited neurotization of the distal stump was obtained.

April 14, 19119.

DISCUSSION

Lt. Col. Dean Lewis: We are to be congratulated on having this paper presented at the present time when so many peripheral nerve injuries are being treated. There is one thing that I think has been definitely demonstrated; namely, that all regeneration takes place from the proximal stump. I also believe that it has been definitely proven that without protoplasmic bands no regeneration takes place. That is illustrated in section of the spinal cord or in section of the optic nerve. I believe all peripheral nerve surgery should be taken care of in evacuation hospitals and that in all cases primary suture should be done. It is exceedingly interesting to study peripheral nerve injuries in the evacuation hospital, say fifteen hours after injury. In all the cases I have seen, either from high explosives or machine gun bullets. the nerves immediately after section have been found contused. A machine gun bullet may make a perfectly clean hole, but if one examines the peripheral nerves, one finds on each side of the defect for a half inch that all elements of the nerve are destroyed. So if an attempt is made to make suture considerable approximation must be accomplished to get neurofibrilla in contact with neurofibrilla. In the musculo-spiral it is practically impossible to approximate these without flexion of the elbow, or in the sciatic without flexion of the knee to a right angle.

There has never been much opportunity to study these nerves that had primary suture. It is unfortunate that the primary sutures at the evacuation hospitals are so distributed in this country that it is impossible to make a study. At Fort Sheridan I have found only one case of extensive primary suture. Quite a number of the cases, in fact, the majority of them, have had a separation of the nerve ends with a neuroma. They have had complete loss of function primarily, but they have gradually improved. Now, six or seven months after the injury, we find that this preliminary return of function has come to a stationary point. I operated on two cases this morning, which had improved rapidly for some time, but for the last three months had been stationary. In examining one of these cases, which was the sciatic, I found just a few adhesions. The only thing was to excise the neuroma and attempt a neurolysis and suture the healthy muscle above and below and wait for return of function. The second case I operated on this morning had what was theoretically a complete ulnar lesion and a partial median lesion. The ulnar had a very distinct lesion of the nerve with some of the funiculi destroyed, and yet there were enough funiculi left to conduct the impulses through.

The median was bound in scar tissue. It was merely an indication for neurolysis. There are very many cases with division of both nerves. The most serious are the lesions in the arm in which the median and ulnar are divided. It is surprising that an ulnar lesion alone is less frequent than an ulnar combined with a median. If you flex the forearm to get an end-to-end suture of the separated ends of the ulnar, it is difficult to handle the median. It is much better to make and end-to-end suture of the median and to transplant in the ulnar than to sacrifice the ulnar by doing some other operation on the median. There is no doubt but that the ideal nerve repair is end-to-end suture and that it should be attempted in all cases. To resect the humerus in order to make an end-to-end suture of the median or the ulnar in my opinion should never be done. In lesions of the sciatic of over 2½ inches' defect, one can flex the knee to a right angle, immobilize, and close the defect. In the case of the ulnar just above the wrist-joint, it is practically impossible to close any defect by flexion of the wrist. In these cases the autotransplant ought to be used. In most of these cases you can get an autotransplant directly from the site of your operation. For instance, in the case of the median or ulnar, you can use the cutaneous branch. I think that is the operation of choice. In cases where you cannot well sacrifice the cutaneous nerve, I think a man is justified in using some form of tubulization, using either a formalized artery or a fascial tube. A fascial tube has a distinct limitation in all these injury cases, because a fascial tube transplanted in the presence of scar tissue will become scar tissue. That is the fate of fascial tubes in all these wounds.

I think we have three things to take into consideration. First, primary end-to-end suture on those cases with small nodules in the nerve. Then linear section and autoneurolysis with the idea of allowing the nerve to expand to allow the nerve axones to grow through. Second, combined with this, the operation in which one dissects off the scar tissue. Third, if one cannot bridge the defect, an autotransplant should be used.

In all these nerve operations we must consider the after-treatment. There are some sad things happening in war surgery by overemphasis of certain points. Thomas, years ago, said that all paralyzed muscles should be placed at rest. We heard for many years about the cocked-up splint for musculo-spiral paralysis. Now some of these boys have worn the cocked-up splint for the cure of drop-wrist for so long that they have an ankylosis of the wrist. It is just as harmful to overstretch healthy muscles as it is to maltreat

a paralyzed muscle. To make a primary suture is by no means to finish the case. The after-treatment is most important in the correction of the paralysis.

Another thing sometimes forgotten is that up to the present time we have not had the opportunity of studying the results of our operations on nerves. I do not believe we can say anything about the return of function in these cases, even in the musculo-spiral or popliteal, for at least seven months. It would be very unfortunate if any of these wounded men were discharged before the period has expired in which we can expect a regeneration, because if we are going to learn anything in the line of peripheral nerve surgery from this war, these men must be watched for at least two years before we can make definite statements in regard to operations on peripheral nerves.

Major Lewis J. Pollock said that statistics relative to the incidence of peripheral nerve lesions sustained in battle were not as yet available. Those obtained from reports of the American Expeditionary Forces were not reliable for the reason that many cases of peripheral nerve lesions were not referred to the neurologist. As a result a large number of cases suffering with severe wounds, or those requiring complicated dressings were not observed from the neurological standpoint. As consultant to a number of base hospitals, Major Pollock had between thirty and fifty such cases referred to him during a month from each of these hospitals. A survey made of the cases brought to his attention on September 7, 1918, when the population of the hospital under investigation was 1,440, revealed forty cases, or a percentage of 2.77.

In the early part of November, 1918, the total figures submitted to the chief consultant in neuropsychiatry led him to believe that the percentage of peripheral nerve cases in the American army was 1.76. This did not approach the figures given by the French and British, which were nearly 6 per cent. At this time a bed-to-bed examination of all cases wounded in extremities was made and in four hospitals under Major Pollock's supervision it was found that of 2,130 cases examined, 332 had peripheral nerve lesions. The total population of these hospitals at that time was 7,050. The percentage of peripheral nerve lesions in the total population was 4.5. The percentage of peripheral nerve lesions as to cases examined was 14.9.

Analyses of the types of lesions seen were inaccurate for similar reasons. The prominence of certain clinical symptoms in some injuries made it necessary to submit such a case to the neurologist, so that ulnar lesions were very fre-

quently referred to the neurologist, whereas median lesions were frequently overlooked. Internal popliteal lesions were rarely referred to the neurological department.

The lack of standard nomenclature often contributed to the reports of internal popliteal lesions where a partial sciatic lesion was present.

The striking feature of the clinical picture of early nerve lesions was the large percentage of marked and rapid improvement. An analysis of the first 100 cases seen in Base Hospital No. 13 showed that after three months sixty-one cases had been discharged. Twenty of these cases had sufficiently recovered to be sent to convalescent and replacement camps. Thirty-nine cases remained in the hospital; twenty of these were manifestly partial lesions and only five were so severe as definitely to indicate the necessity for surgical interference.

The actual percentage of recoverable cases of peripheral nerve lesions can only be ascertained when accurate statistics of the cases suffering with disability as the result of a peripheral nerve lesion may be compared to statistics of the occurrence of peripheral nerve lesions in battle. It might be mentioned that probably 10,000 peripheral nerve lesions were sustained in battle. Not very many more than 3,000 cases had been classified as peripheral nerve cases in the hospitals in the United States. Only one-third of the cases observed in the United States General Hospital No. 28, Fort Sheridan, Illinois, would require operative interference, and of these cases but the smaller proportion would require nerve suture.

April 14, 1919.

THE AGGLUTINATION OF HUMAN ERYTHROCYTES BY HORSE SERUM

M. S. TONGS

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Williams and Patterson[1] found that horse serum frequently agglutinated human erythrocytes in the test tube. Of the nineteen horse serums, nine normal and ten immunized, they tested, twelve agglutinated half or more of the samples of blood in dilution of 1:20; and ten, in dilution of 1:50. Two serums agglutinated

1. The Jour. A. M. A., 1980, 70, p. 1754.

TABLE 1.—THE AGGLUTINATION OF HUMAN ERYTHROCYTES BY NORMAL HORSE SERUM

Human Erythrocytes	Normal Horse Serum																			
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
1	0	1:20	1:20	1:20	0	1:20	1:10	0	1:20	1:20	0	1:20	1:20	1:40	1:20	1:20	1:20	1:20	1:20	1:20
2	0	1:20	1:20	1:20	0	1:20	1:10	0	1:20	1:20	1:40	1:20	1:20	1:40	1:20	1:20	1:20	1:20	1:20	1:20
3	1:10	1:20	1:10	1:20	0	1:20	1:10	0	1:20	1:20	1:40	1:20	1:20	1:40	1:20	1:20	1:20	1:20	1:20	1:20
4	1:20	1:20	1:20	1:20	0	1:40	1:10	0	1:20	1:20	1:40	1:20	1:20	1:40	1:20	1:20	1:20	1:20	1:20	1:20
5	1:20	1:20	1:20	1:20	0	1:20	1:10	0	1:20	1:20	1:40	1:20	1:20	1:40	1:20	1:20	1:20	1:20	1:20	1:20
6	0	1:20	1:20	1:20	0	1:20	1:10	0	1:20	1:20	1:40	0	1:20	1:40	0	0	1:20	1:20	1:20	1:20
7	1:20	1:20	1:20	1:20	0	1:40	1:20	0	1:20	1:20	1:40	1:20	1:20	1:10	1:20	1:20	1:20	1:20	1:20	1:20
8	1:20	1:20	1:10	1:20	0	1:40	1:10	0	1:20	1:20	0	1:20	0	1:40	1:20	1:20	1:20	1:20	1:20	1:20
9	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
10	1:20	1:20	1:20	1:20	0	1:40	1:10	0	1:20	1:20	0	1:20	1:20	1:40	1:20	0	1:20	1:20	1:20	1:20
11	1:40	1:20	0	0	0	0	1:10	0	0	1:20	1:40	1:20	1:20	0	1:20	0	1:20	1:20	1:20	0
12	1:20	1:20	1:20	1:20	0	1:20	1:10	0	1:20	1:20	0	1:20	1:20	1:40	1:20	1:20	1:20	1:20	1:20	1:20
13	1:10	1:20	1:20	1:20	0	1:20	1:20	0	1:20	1:20	1:40	1:20	1:20	1:40	1:20	1:20	1:20	1:20	1:20	0
14	1:10	1:20	1:20	1:20	0	0	1:10	0	0	1:20	1:40	1:20	1:20	0	1:20	0	1:20	1:20	1:20	1:20
15	1:20	1:20	1:20	1:20	0	1:20	1:10	0	1:20	1:20	1:40	1:20	1:20	1:40	1:20	0	1:20	1:20	1:20	1:20
16	1:10	1:20	1:20	1:20	0	1:20	1:10	0	1:20	1:20	1:40	1:20	1:20	1:40	1:20	1:20	1:20	1:20	1:20	1:20
17	1:20	1:20	1:20	1:20	0	1:20	1:10	0	1:20	1:20	1:40	1:20	1:20	1:40	1:20	1:20	1:20	1:20	1:20	1:20
18	1:20	1:20	1:20	1:20	0	1:20	1:10	0	1:20	1:20	1:40	1:20	1:20	1:40	1:20	1:20	1:20	1:20	1:20	1:20

each two different specimens of blood in dilution of 1 : 20 and one showed slight but definite agglutination in dilution of 1 : 500.

I have tested twenty normal horse serums and seven antiserums produced from the horse and containing preservative. The blood specimens were obtained from dispensary patients and collected in 1 per cent. sodium citrate in physiologic salt solution, centrifuged and washed three times. The dilutions of serum were from 1-10 to 320. Each tube contained 1 per cent. suspension of human red corpuscles and serum in the desired dilution in equal quantity. In each case control tests were made. The tubes were thoroughly shaken and incubated at 37 C. for one hour. The results were usually read about one hour after removal from incubator with the naked eye and under the microscope. In both cases the readings agreed well. Two normal and two immune serums did not agglutinate any of the samples of blood, and all the serums failed to agglutinate human red blood corpuscles No. 9. The results are given in the table.

TABLE 2.—THE AGGLUTINATION OF HUMAN ERYTHROCYTES BY ANTIDIPHTHERIA SERUM (HORSE)

Human Erythrocytes	Antiserum						
	1	2	3	4	5	6	7
1	1:20	0	0	1:20	1:40	1:20	1:20
2	1:20	0	0	1:20	1:40	1:20	1:20
3	1:20	0	0	1:40	1:40	1:20	1:20
4	1:20	0	0	1:40	1:40	1:20	1:20
5	1:20	0	0	1:20	1:40	1:10	1:20
6	1:20	0	0	1:20	1:40	1:20	1:20
7	1:20	0	0	1:20	1:40	1:20	1:20
8	1:20	0	0	1:20	1:40	1:20	1:20
9	1:20	0	0	1:20	1:40	1:20	1:20
10	1:20	0	0	1:20	1:40	1:20	1:20

CONCLUSION

Horse serum usually contains a moderate amount of agglutinin for human blood corpuscles; the sensitiveness of the red corpuscles of different individuals to the agglutinin varies considerably.

May 12, 1919.

HYPERPLASTIC PYELITIS AND URETERITIS CYSTICA

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The description of this disease by most authors is accredited to Litten,* who made the first accurate account of it, but it was previously observed by Morgagni,[1] Rayer[2] and Rokitansky.[3] From time to time it has been splendidly described by many authors as R. von Limbeck,[4] Silcock,[5] Eve,[6] Clarke,[7] von Kahlden,[8] Lubarsch,[9] Stoerk[10] and Giani.[11]

Early observers believed the linings of the renal pelves and ureters have true glands and that the cysts which form such a conspicuous feature of the disease are due to retention. The absence of glandular structures in these parts, however, was demonstrated by Marchwald[12] (1898). Others, as von Kahlden, Eve and Clarke have suggested for its eitology an infectious process, certain variously shaped, granular bodies found inside of the cysts being regarded as protozoa. But no one as yet has found any of the supposed protozoa in or among the epithelial cells of the mucous membrane of the genito-urinary tract, or the cells lining the walls of these cysts, and parasites from these cysts have not been artificially cultivated. The disease has not been reproduced by inoculation of the cyst content into lower animals. Others have suggested that cysts of the lining of the urinary bladder

* Virchow's Archiv., 66, 139; cited by von Kahlden.

1. De Sedibus et Causis Morborum, epist. 28, Art. 41. Cited by von Kahlden.
2. Traité des Maladies des Reins, Paris, 1841, 3, 560. Cited by von Kahlden.
3. Lehrbuch der Speziellen Path. Anat., 1861, 3, 354.
4. Ztschr. f. Heilk., 1887, 8, 55, cited by Stoerk.
5. Trans. Path. Soc. London, 1889, 40, 175-176.
6. Trans. Path. Soc. London, 1889, 40, 444-446.
7. Trans. Path. Soc. London, 1892, 43, 94-99.
8. Beitr. z. path. Anat. u. allg. Patb, Jena, 1894, 16, 561-593.
9. Archiv f. Mikrosk. Anat,, 1893, 41, 303, cited by Stoerk.
10. Beitr. z. path. Anat. u. allg. Path., Jena, 1911, 50, 361-397.
11. Beitr. z. path. Anat. u. allg. Path., Jena, 1907, 42, 1-23.
12. Cited by Soerk.

may be due to misplaced prostatic glandular tissue. Age does not seem to be a factor. Stow,[13] has suggested a congenital malformation as a cause.

It is the opinion of most writers that the formation of these cysts has a definite relation to chronic irritation of the lining mucous membrane. This opinion is supported in the work of Giani, who experimentally by suprapubic cystotomy upon rabbits placed within the urinary bladder some gelatin capsules which later became the centers of larger calculi. The rabbits were killed at intervals between forty-eight hours and 178 days. In the bladder of those killed after two weeks there was chronic cystitis. In numerous places of the mucous membrane at this time there was a marked tendency toward proliferation of the epithelial cells, as sprouts dipping down into the deeper layers, or as separate islands of epithelial cells. Because of the proliferation of the peripheral cells of the islands or sprouts, the central cells underwent pressure and liquefaction necrosis. This resulted in cyst-like formations which became larger by further proliferation of the peripheral cells with subsequent central liquefaction necrosis. This occurred about the fortieth day. The content of a cyst was a fine, granular detritus of red blood cells. It was this material which was confused with protozoa by earlier observers. About the one hundredth day these cysts were macroscopic. Because of further pressure from within and the gathering-in of fluid, the lining of the cysts in the lumen of the bladder gradually became thinned until they finally ruptured. The walls of the ruptured portions disintegrated and the base assumed the normal epithelial lining of the bladder. At the two-hundred and seventieth day the cysts all had disappeared without a trace being left behind. Giani concludes (1) that any cause which for a certain length of time induces a vigorous proliferation of the bladder epithelium may produce at the same time these epithelial nests; (2) the evolution of these cysts in their later stages is independent of the primary irritation.

13. Annals of Surgery, 1907, 46, 233 243.

If inflammatory irritations of the mucous membrane of the genito-urinary tract set up a proliferation of its epithelial surface so that sprouts and cell-nests develop, out of which cysts later are formed, it is difficult to reason why these cysts are not more common, for apparently only fifty cases have been reported in the literature.

Clinical History.—I. A., Italian, single, age 25 years, was brought to the Cook County Hospital, May 8, 1918, to the service of Dr. Post. He was semi-comatose on admission. The breathing was stertorous, the pulse 104, the temperature 97, the respirations 36. The blood pressure was systolic 130, and diastolic 90. The pupils were equal and reacted to light. On auscultation of the lungs there were a few bubbling râles. The urine contained much albumin, red blood cells, pus cells, and casts. The spinal fluid was under slightly increased pressure and contained thirty cells per cm. The past history was negative. Death occurred the following day, May 9, 1918.

Anatomic Diagnosis (Dr. E. R. LeCount).—Calculus in the urinary bladder; bilateral hyperplastic pyelitis and ureteritis cystica; greatly dilated ureters and renal pelvis; pressure atrophy of the kidneys (uremia); marked edema of the brain; foramen magnum pressure furrow of the brain stem; slight bronchopneumonia of the right lung; marked hyperplasia of the spleen, moderate of the lymphoid nodules of the ileum; lessened yellow material of the adrenal cortices; moderate acute emaciation; passive hyperemia and edema of the lungs; moderate passive hyperemia of the liver; sordes of the lips; petechial hemorrhages into the lining of the stomach (cardiac antrum); passive hyperemia of the leptomeninges; slight fatty changes of the aorta, and carotid arteries; lumbar needle-puncture wounds.

The lining of the right ureter is roughened by hundreds of grey to pink, opaque, soft, spherical cysts, 2 to 6 mm. in dia., containing serous, turbid fluid (see figure). They are freely moveable and attached to the lining of the ureter by a narrow membranous pedicle. They are most numerous 7.5 cm. proximal to the junction of the ureter with the bladder. Here they occupy the entire lining, which is 4 cm. in dia., their sides firmly approximated, and practically occlude the lumen.

In the pelvis of the right kidney there are sixty-six similar cysts, most of them larger than those of the ureter. They occupy about three-eighths of the whole lining of this ureter and pelvis of this kidney. Where the mucosa is not rough-

ened with cysts there are pin-head size nodules which mottle this surface.

The lining of the left ureter and pelvis of the kidney contain similar cysts, more numerous, but not so large generally as those of the right. These are also closely grouped together and occupy altogether about two-thirds of the lining of this ureter, and partially obliterate the lumen which is uniformly about 3 cm. in dia. The cysts are of the mucosa of the ureters and renal pelves only.

The calices of both kidneys are distended to about four times their normal size, and the kidney parenchyma is proportionately reduced. The cortex is 3 to 9 mm. thick, the pyramid 6 to 10 inches.

On microscopic examination with serial sections the changes are essentially similar to those described by other observers.

This specimen is like those previously described but differs from them in that none, so far as I have been able to find, have been described in which the disease was so extensive, or the cysts so large and numerous.

May 12, 1919.

ANEURYSM OF THE ROOT OF THE AORTA AND ITS RELATION TO CORONARY CIRCULATION

H. A. OBERHELMAN

From the Pathological Laboratory, Rush Medical College, Chicago

Under the title "Dissection of the Heart by an Aneurysm of the Aortic Root,"[1] Dr. Grayston, then a resident physician of the Cook County Hospital, reported among other details a large aneurysm of the aorta which had been studied clinically for a number of years with total obliteration of the right coronary artery.

Dr. E. R. LeCount has recently referred to the development of collateral circulation between the two coronary arteries[2] when the interference with the circulation is gradually brought about.

1. Cook County Hospital Reports, Chicago, 1906, p. 280.
2. Pathology of Angina Pectoris, Proceedings of the Institute of Medicine of Chicago, 1918, 2, p. 65, and Angina Pectoris, p. 77.

In the heart I have to demonstrate, the small aneurysm of the aortic root is so located that some interference with the circulation in one of the coronary arteries must have been exerted for some time before death.

This heart was taken from a man 50 year old who was found, June 1, 1918, at 5:15 p. m., on the street by a police officer, where he had fallen, bruised himself and become unconscious. He was taken at once to the Cook County Hospital to the service of Dr. Eisendrath in a condition of marked cyanosis, with shallow breathing and an imperceptible pulse. The examining physician found no heart murmurs and the heart borders were reported normal; within an hour he died.

The heart weighs 340 grams and the greatest transverse diameter is 14.5 cm. The apex is made up entirely of the left ventricle which has a wall at the base 1.8 cm. thick, at the middle 1.6 and at the apex 1.1. The cavity of the left ventricle is 7.6 cm. long. The lining of the ventricles, pulmonary arteries and veins and the coverings of the tricuspid and mitral leaflets and pulmonary and aortic cusps are all smooth and unchanged. The tricuspid ring is 11.5 cm. in circumference, the mitral 9, the pulmonary 6.8, the aortic 8. The foramen ovale is closed. The Eustachian valve is an intact membrane 36 cm. long and 4 wide. The Thebesian valve is represented by two aberrant bands stretched across the opening of the coronary sinus, the longer 1.4 cm. The epicardium is thin, glistening and translucent. There is only a moderate amount of pale yellow and finely lobulated epicardial fat and this chiefly along the course of the coronary arteries and atrio-ventricular groove. The ascending aorta is tightly adherent to the superior vena cava by fibrous tissue and here in places the lining of the superior vena cava is wrinkled. The lining of the proximal 4 cm. of the aorta is rough with silver-grey wrinkled thickenings (Fig. 1 A) involving practically the entire lining. Here there are also about eight yellow, firm places (Fig. 1 C), the largest 13 mm. in dia., all of which contain lime. There is an accessory left coronary artery (Fig. 1 D) with a mouth 1 mm. in dia. Only the mouth is patent, the rest of the artery lies obliterated in the wall of the aneurysmal sac. The mouth of the left coronary artery (Fig. 1 E) is reduced in diameter by the thickening of its own lining and that of the aorta. The lumen of this artery for 4 cm. where it lies close to the wall of the

aneurysmal sac (Fig. 2 A) is more than two-thirds compressed. Elsewhere the branches of this artery are without gross or microscopic change. The mouth of the right coronary artery (Fig. 1 F) is lessened a little in diameter by syphilitic involvement of the lining of its mouth and that of the aorta near it. Elsewhere the channels of this artery and that of its branches are without change.

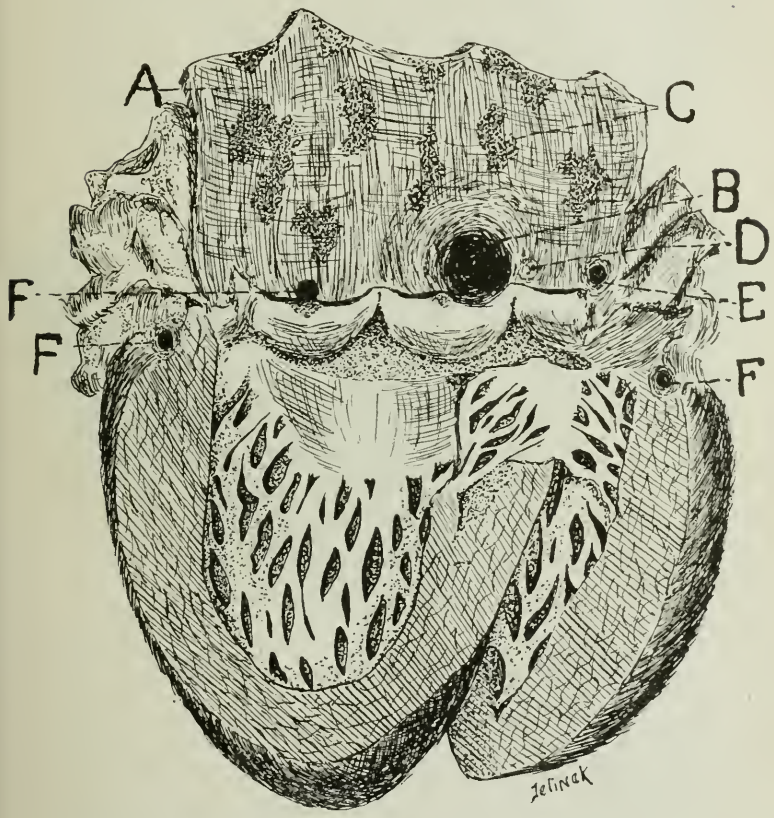

Fig. 1.—Left side of heart and aorta opened, showing mouth of aneurysm. A. Syphilitic aortitis. B. Mouth of the aneurysm. C. Senile sclerosis of the aortic lining. D. Mouth of an accessory left coronary artery. E. Mouth of the left coronary artery. F. Right coronary artery.

There is a sacculated aneurysm (Figs. 1 B and 2 B) jutting out from the root of the aorta at the posterior sinus of

Valsalva where it opens by a round operture 1.6 cm. in dia. with thick rough and pearly-grey margins. The mouth of this aneurysm has entirely replaced the left two-thirds of this posterior sinus of Valsalva, and it is also directly above the right half of the upper attachment of the front mitral leaflet. The aneurysmal sac is 3.8 cm. side to side, 2.2 front to back and 3.3 up and down. It projects back and a little to the right (Fig. 2 B) so that there is a bulging into both auricles, somewhat more into the right than the left. The bulging into the right auricle is 3.6 up and down, 3 front to back and 1.7 side to side. At the lower front margin of this bulging of the right auricular side and also 8 mm. above the junction of the posterior and medial tricuspid leaflets (not

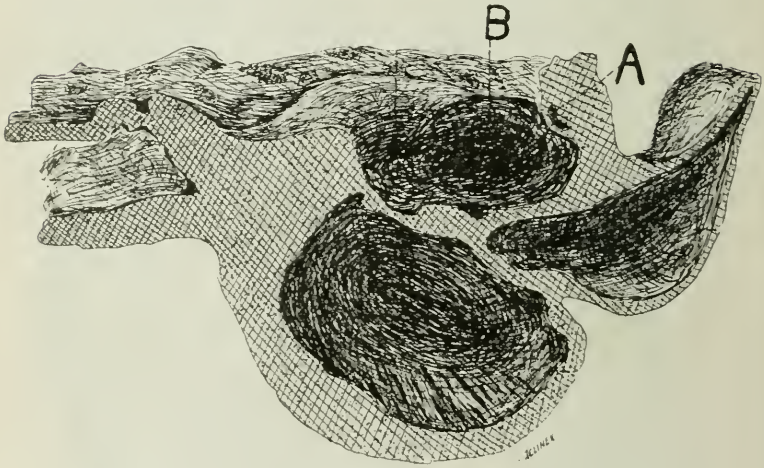

Fig. 2.—Cross section of heart at base of the aorta and through the center of the aneurysm. A. Compressed left coronary artery. B. Interior of the aneurysmal sac.

shown in the figures) there is a perforation 7 mm. in dia. with sharp margins where the rupture of the aneurysm into the right auricle had occurred. The front wall of this aneurysm is formed by the base of the posterior cusp and interauricular septum, the back wall by the greatly dilated aortic root, and the base and sides by the inner walls of the two auricles.

Microscopic examination of the apex, middle and septum of the myocardium reveals no increase of fibrous tissue anywhere. In the wall of the aorta and aneurysmal sac there are definite syphilitic changes.

CONCLUSION

In this case there can be no doubt that gradual compression of the left coronary artery adjacent to the aneurysmal sac had been present for some time before death. This produced unquestioned interference with coronary circulation. Therefore, it would seem quite reasonable to assume, because of the absence of microscopic change in the myocardium, that collateral circulation between the right and left coronary arteries is established with gradual interference with the circulation in one or other artery.

May 12, 1919.

SUMMARY OF OBSERVATIONS IN TESTS FOR ALBUMINURIA

LUDVIG HEKTOEN

AND

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This summary is based on results of urinary examinations at frequent intervals and with various methods in scarlet fever and diphtheria. The methods used were the heat-acid test, the potassium ferrocyanid test, Leone's test, Spiegler's test, and the precipitin test with antihuman rabbit serum.

The ferrocyanid test was made in this way: In a small tube is placed 0.25 c.c. of filtered urine and the same amount of a 10 per cent. ferrocyanid solution introduced at the bottom with a fine pipet; now one or two drops of glacial acetic are run down the sides of the tube. As the acid sinks a sharply defined ring forms at the junction of the ferrocyanid and the urine if the latter is albuminous. This test is said to react positively in protein dilutions up to 1-50,000, but it also reacts with proteoses.

In Leone's[1] test the reagent contains several protein precipitants (potassium dichromate, acetic and sul-

1. Leone, R.: Acetic-sulphuric acid test for albumin, Policlinico, 1918, 25, p. 224; Abst. in J. A. M. A., 1918, p. 1340.

phuric acids) and is claimed to react with protein in dilutions as high as 1-180,000. This is the most delicate chemical test and is made by the contact method.

In Spiegler's[2] test a slightly acid mercuric chlorid solution is used which precipitates not only proteins but also amino acids and amines. It is about as sensitive as the ferrocyanid test.

The precipitin test is made with filtered, neutralized urine in small, absolutely clean tubes; about 0.1 c.c. or so of antihuman rabbit serum is introduced at the bottom with a fine pipet in such a way that the two fluids come into contact without being mixed; the tubes are left at room temperature for an hour or so. If unchanged human protein is present a ringlike layer of finely granular grayish-white precipitate forms at the junction of the two fluids. The ultimate sensitiveness of this test depends on the precipitin strength of the antihuman serum as measured by the dilution of human serum or blood in which it causes precipitation.

As measured by the highest dilution of albuminous urine in which positive reactions developed, the heat-acid test is the least sensitive of these tests and the precipitin test the most sensitive, provided, of course, that the antiserum is highly potent. Occasionally in cases of mild nephritis, usually of some standing, the ferrocyanid and Spiegler tests only gave positive results, probably because these tests give reactions with products of protein-splitting which do not react in Leone's test or with specific precipitins.

The precipitin test being like the anaphylactic reaction,[3] a test for species proteins in general, can give no information as to the source of protein in the urine, whether from the blood or the cells of the kidneys.

Albuminous urine from cases of diphtheria treated with serum (horse) in no case reacted with potent antihorse precipitin serum, showing, as Cameron and Wells[4] have shown by means of the anaphylactic reac-

2. Spiegler, Edw.: Eine empfindliche Reaktion auf Eiweiss im Harne, Wien. klin. Wchnschr., 1892, 5, p. 26.

3. Wells, H. G.: Observations on alimentary albuminuria by means of the anaphylactic reaction, J. A. M. A., 1909, 53, p. 863.

4. Cameron, A. L., and Wells, H. G.: The origin of the proteins of nephritic urine. Arch. Int. Med., 1915, 15, p. 746.

tion, that foreign proteins introduced into the body do not reach the urine as such.

Repeated examinations of the urine with refined methods did not give any better indications of oncoming nephritis than the usual clinical tests; only a small number of cases of nephritis developed, however, and more extended observations may lead to other results.

May 12, 1919.

PRELIMINARY STUDIES ON THE INFLUENCE OF ALCOHOL AND NICOTIN ON THE OVARY

SUKEMASA OGATA

From the Otho S. A. Sprague Memorial Institute and Pathological Laboratory, University of Chicago

Six young rabbits were injected intravenously in the ear vein with 40 per cent. alcohol every two to four days with gradually increasing doses from 4 c.c. to 8 c.c. The left ovary was removed in each animal three to five days before the first injection. From nine to twenty injections were given, the total amount of alcohol administered varying from 48 c.c. to 123 c.c. The total period of injection varied from thirty-one to seventy-six days. Corresponding sections of the normal and alcoholized ovaries were compared.

The extract of nicotin was prepared by adding 50 c.c. of physiologic salt solution to 1 gram of cigar tobacco. After standing for twenty-four hours, it was filtered through a Berkefeld filter and used for injection. Four rabbits were injected intravenously in ear veins once every two to four days with doses of the extract gradually increasing from 3 to 5 c.c. The total period of treatment varied from thirty-five to sixty-four days, from eleven to twenty-two injections having been given, the total quantity of the extract given having been from 29 to 62 c.c.

No particular changes were found in the structure of the graafian follicles and stroma of the ovaries of

rabbits treated with either alcohol or nicotin extract, although in some of the animals exposed to the repeated alcohol injections, there was an apparent reduction in the number of developing graafian follicles.

May 12, 1919.

CAPT. GEORGE SCHRADER MATHERS

LUDVIG HEKTOEN

Capt. George Schrader Mathers, M. C., U. S. Army, a member of the staff of the McCormick Institute for Infectious Diseases, Chicago, died Oct. 5, 1918, at the age of 31.

Captain Mathers took his college work in the University of Texas and the University of Chicago, and received his medical degree from Rush Medical College in affiliation with the University of Chicago in 1913. Having served one year and a half as intern in the Cook County Hospital, he began work in the McCormick Institute under a grant from the Fenger Memorial Fund, but before long he became associated fully with the institute. During the three and one-half years of this association he accomplished much fruitful work and published important papers on lobar pneumonia, epidemic poliomyelitis, acute respiratory infections in man and in the horse, and on epidemic meningitis. He demonstrated that a streptococcus-like micro-organism occurs apparently constantly in the central nervous system in persons that have died from epidemic poliomyelitis. Early last spring he was commissioned as first lieutenant and placed in charge of the laboratory of the embarkation hospital at Camp Stuart. In May he was promoted to captain and given charge of the laboratory of the base hospital at Camp Meade. He gave himself completely to his work. In the course of his duties and while intensely engaged in a study of the bacteriology of influenza he was stricken and died with pneumonia in a few days.

Captain Mathers was a fine, lofty-minded, lovable young man, of rare enthusiasm for work and a remarkable efficiency. He had committed himself to research and his early death is a great loss to medicine.

TRANSACTIONS OF THE CHICAGO PATHOLOGICAL SOCIETY

VOL. XI. FEBRUARY 1, 1920. NO. 2

CHORIO-EPITHELIOMA OF THE TESTIS

HARRY JACKSON

Marchand,[1] in 1895 clearly defined the entity of chorio-epithelioma and differentiated it from deciduoma, by showing its origin from the chorion alone. Marchand stated at that time that chorio-epithelioma was distinctly a tumor occurring only in the female in connection with pregnancy. Since then it has been shown that tumors of morphologic characteristics similar to chorio-epithelioma of pregnancy may occur in the female in connection with teratoma unassociated with pregnancy.[2]

That similar tumors could occur in the male was not known until 1902, when Schlagenhaufer[3] described very accurately a chorio-epithelioma of the testis and found five other instances of this neoplasm in the collection of the Vienna Museum, which had been diagnosed as mixed tumor of the testis, sarcoma angio-plastique, embryoma, etc. Since 1902 I have collected eighty-two cases, including sixty-seven cases collected by Woglom[4] in 1917, and fourteen cases recently reported by Hartman[5] and one of my own. Almost half of these cases have been reported in the last four years, showing that the condition is being recognized much more frequently than formerly.

1. Ueber die sog. "decidualen" Geschwülste, Monatsschrift für Geburtshilfe und Gyn. 1, Heft 5 und 6, 1895.
2. Frank: J. A. M. A. **56**: 248, 1906
3. Wien. klin. Wchnschr. Nr. 22 u. 23, 1902.
4. St. Lukes Hosp. Med. and Surg. Reports, New York, **4**: 188, 1917.
5 Bull. de l'Acad. de Med., Paris, June 3, 1919.

Ewing has been largely instrumental in directing attention to the mixed tumors of the testis, showing that 80 per cent. of them contain more than two varieties of tissue, and in reality are teratomas. The diagnosis of a teratoma may be obscured by the fact that one tissue may overshadow the others in growth. When a chorio-epithelioma complicates a teratoma of the testis its appearance is indicated by the presence of masses resembling old and recent blood clot. Microscopic examination of this material will show typical areas of syncytial tissue with the large wandering chorionic cells whose lytic action allowed them to penetrate the large blood sinuses and produce distant metastases in the lungs, liver, etc. Langhans cells are also present as large polyhedral cells with a small nucleus and cytoplasm rich in glycogen.

Recently Hartmann has attempted to differentiate a type of neoplasm which he designates a placentoma (hydatid mole?) composed of chorionic cells of adult type as distinguished from choriomas—composed of chorionic cells of embryonic type. It is interesting to note that in two cases of chorio-epithelioma of the testis reported by Warthin and Cooke,[6] respectively, there exisited a hypertrophy of the breast and secretion of colostrum.

The personal case herewith included occurred in a young man 22 years of age. The main tumor of the testis was a teratoma present for four years and during the last three months the upper portion became malignant, as a chorio-epithelioma, and produced metastases in the lungs and liver. It is reported in detail in *The Journal of the American Medical Association*, Dec. 20, 1919.

Oct. 13, 1919.

6. Bull. Johns Hopkins Hosp. **26**: 215, 1915.

DIFFUSE OSTEOPLASTIC CARCINOMA OF THE BONES

PETER BASSOE

AND

BURRELL O. RAULSTON

From the Pathological Laboratory of the Presbyterian Hospital, Chicago

While carcinoma of the prostate with extensive metastases in the bones is a common occurrence, the instance presented here is considered sufficiently unique to justify recording it alone.

The patient, a man 59 years old, entered the Presbyterian Hospital on Nov. 8, 1918, complaining of pain and tenderness about his joints, both in the upper and lower extremities. While he had suffered from this from time to time for twenty years, it had not been severe until a tonsillectomy was performed in February, 1918. Since that time he had lost 71 pounds in weight. He complained of marked general weakness. There was no general history of joint swelling at any time.

Aside from general emaciation and a somewhat cachectic appearance, the most striking point in the examination was the presence of marked tenderness of certain bones, especially the ribs, clavicles, humeri, sternum, scapulae, vertebrae, and iliac bones. The bones of the forearm and of the legs were not tender. There was no muscular tenderness. The tendon reflexes and the plantar and cremasteric reflexes were normal. The abdominal reflexes were not obtained. Later slight patellar and ankle clonus was obtained on the right side. There was no paralysis and no local muscular atrophy. There was no sphincter disturbance. A few enlarged and indurated inguinal glands were noted. Routine examination of the blood gave the following results: Hemoglobin, 56 per cent.; red cells, 3,900,000; white cells, 2,600. Differential count of 100 cells: Small lymphocytes, 7; large lymphocytes, 2; large mononuclears, 16; polymorphonuclear neutrophils, 61; eosinophils, 4; myelocytes, 4; unclassifiable, 5. A second blood count three weeks later gave: hemoglobin, 30 per cent.; red cells, 1,980,000; white cells, 8,200. Repeated examination of the urine for Bence-Jones protein was negative.

At the time of this examination no deformity of the bones could be detected. Roentgen-ray plates were made, however, and it was found that all those bones that were tender on pressure produced marked, extensive mottling of the shadows

cast by them, apparently because of irregularity of calcification. The appearance strongly suggested metastatic carcinoma.

One of the indurated inguinal glands was removed and by histological examination a diagnosis of adenocarcinoma was made.

By further roentgen-ray examination there were found marked changes in the iliac bones, and the seventh and eighth ribs on both sides, which were particularly tender, presented mottling and fusiform enlargement. There was no distinct evidence of decalcification either in the skull or spinal column.

The prostate gland was found to be asymmetrical, the left lobe being somewhat larger than the right, firmer, and slightly nodular. The findings were not considered typical of carcinoma, but rather suspicious. Repeated examination of the urine was negative, and there was no difficulty in micturition.

On the use of sodium cacodylate, the patient improved temporarily, but later gradually lost in weight and strength. He left the Hospital, Feb. 14, 1919, with the clinical diagnosis of carcinomatosis of the bones and probable primary carcinoma of the prostate. He developed symptoms of urinary obstruction after leaving the hospital, and cystitis was included in the diagnosis at the time of death. At home he was under the care of Dr. Yorke B. Sutch, to whom we are indebted for the opportunity to make the necropsy.

The patient died, July 18, 1919, and on the same date at necropsy the body was found to be very much emaciated and anemic. Of the superficial lymph glands only those in the inguinal regions were enlarged and they were only the size of small hazel nuts. Owing to the cachectic state of the body, surfaces of the bones of the extremities, clavicles, scapulae and ribs, were easily palpable and were found to be irregular and nodular. There was a large decubital ulcer with a necrotic base over the sacral region. On examination of the organs of the trunk, there was found a marked pyelocystitis, moderate chronic nephritis, senile sclerosis of the aorta and its main branches, fibrous myocarditis and marginal emphysema of the lungs. The prostate was moderately enlarged and surfaces made by sectioning it were gray with yellowish streaks and with striations that resembled fibrous bands radiating from the middle lobe through the lateral lobes at various angles.

The bones that were found to be definitely involved were the vertebrae, the bones of the pelvis, the long bones of both the upper and lower extremities, the sternum ribs, the scapulae and the clavicles. The metastases were less conspicuous in

the spine than elsewhere. A roentgen ray of the spine indicated that the tumor invaded the intervertebral disks to a moderate degree, producing the condition described as "lipping" of the vertebrae.

Parts of the skeleton were removed for further examination. When the soft tissues were removed from the right femur its surface was found to be nodular throughout, the largest nodules being on the lower posterior portion. These nodules were slightly darker than the surrounding bone, were firm and had the appearance of being due to new bone formation.

In histologic sections of the prostate there was found a large amount of compact carcinoma tissue composed of relatively small, round cells. A study of surfaces made by sawing the fixed bone, of histologic sections of the bone, and of roentgen-ray plates made during life and also after the soft parts had been removed, leads to the conclusion that the condition present in the bone is due to metastatic carcinoma there and that the predominating change present is an overgrowth of bone tissue. Grossly and microscopically there can be seen evidence of bone destruction, but this is greatly exceeded by new bone formation.

Of much interest is the fact that the masses of new bone that have been produced here are found to extend through the cortex of the bone and to elevate the periosteum to a marked degree. Many of these regions of hyperplasia have apparently started in the outer portion of the cortex, near the periosteum and have extended outward, pushing this membrane with them. But other nodules are seen that extend from the inner portion of the cortex, near the endosteum, outward sufficiently to elevate the periosteum. Even in osteoplastic tumors of the bone this is unusual.

In histologic sections of these nodules there is relatively a very small amount of carcinoma tissue. In similar sections of the prostate there is an abundant amount of carcinoma, the cells being rather small and compactly arranged. Dr. D. B. Phemister has called our attention to the fact that in his experience the amount of stroma in tumors that produce metastases in bones bears an inverse ratio to the amount found in the secondary growth. That condition is conspicuos in the present instance.

The widespread distribution of metastases in the skeleton of this man with no secondary growths in any other organ, except the inguinal lymph glands, is a good example of the spreading of a tumor by way of the blood stream and the tendency of carcinoma of certain organs to metastasize in special tis-

sues. The large amount of new bone formation and the relatively small amount of tumor tissue associated with it are significant of the power of carcinoma cells to stimulate bone forming tissues to great activity. Whether this power is by purely mechanical or chemical influences, or a combination of these two factors, seems to remain in doubt. Axhausen and von Recklinghausen favor the theory that tumor cells lodge in the capillaries of the bones and by virtue of the hyperemia and mechanical stimulus produced, osteoplastic changes proceed. Statistics indicate that of the metastatic carcinomas of the bones that result from primary carcinoma of the prostate, about 66 per cent. are of the ossifying type.

Oct. 13, 1919.

MULTIPLE BRAIN ABSCESSES SECONDARY TO BRONCHIESTASIS AND KYPHOSCOLIOSIS.

From the Department of Pathology and Bacteriology, University of Illinois, College of Medicine

CLARENCE C. SAELHOF

The etiology of brain abscess is, in approximately 60 per cent. of the recorded cases, due to suppurative condition of the middle ear. Carious processes of the bones of the skull approximate 15 per cent.; abscess secondary to orbital injury, infections, traumatisms, etc., approximate 15 per cent. Abscess secondary to bronchiectasis and lung suppuration approximate 10 per cent.

W. C., aged 30, male, colored, U. S. A. Admitted with diagnosis of Pott's disease and tuberculous meningitis. Patient complains of rigidity of neck and severe pain in the head.

Present Illness.—Patient took sick with headache followed by chill and was bedridden afterward. After the second day, his neck became stiff, which gradually increased. Spasticity of the right leg and right arm with loss of control of the same was evident. There was no vomiting or convul-

sions, but constant sweating. No history of tuberculosis or cancer in his family. He had smallpox ten years previous, gonorrhea two months ago and a hard chancre a few years previous.

The patient attributes present trouble to an accident occurring fourteen years previous to admittance, having been caught at that time in an elevator and claims that his back was broken. He remained in the hospital for only thirty days.

On admittance, increased reflexes, rigidity of the neck, moderate spasticity of the right upper and right lower extremities associated with a stuporous position were evident. Eyes were negative. Kyphosis extended from the tenth dorsal to second lumbar vertebra, with a swelling to the right of the spine in this region about the size of an orange. The patellar reflex was extremely exaggerated on both sides, as was likewise the ankle clonus, Oppenheim, Kernig and Brudzinski reflex.

Wassermann on the blood sera and spinal fluid was negative three times. Spinal fluid contained albumin, no sugar, and 104 lymphocytes per cm. Urine was negative. Blood examination gave Hb of 80, 4,100,000 red and 8,200 white cells.

A tentative diagnosis of poliomyelitis was made. Patient became worse, with increased spasticity of extremities on right side, temperature ranging from 98 to 103.8, and died in a comatose condition nineteen days after admittance.

Necropsy, made by Dr. Davis, gave the following: Bilateral brain abscess; pus in right lateral ventricle; bronchiectasis of the right lung; fibrosis of right lower lobe of right lung; bilateral adhesive pleuritis; left bronchopneumonia; kyphoscoliosis; fetal lobation of both kidneys; chronic localized fibrous peritonitis; alopecia; sacral decubital ulcers; hemorrhoids.

Grossly the different organs appeared practically normal.

Microscopically, the heart musculature appeared in the stage of segmentation and fragmentation; voluntary muscle was normal; kidneys were hyperemic and showed some degeneration; spleen showed hyperplasia of connective tissue and liver showed slight fatty infiltration. Left lung showed bronchopneumonia.

Kyphoscoliosis was present from the tenth dorsal to the second lumbar vertebrae, with an extremely marked deviation to the left, leaving a large cavity in which was wedged the lower right lung and pleura, bound down by dense fibrous adhesions.

The cranial cavity contained an increased amount of cerebrospinal fluid and the meninges were slightly hyperemic. On

section of the brain, four abscesses were found, two in each hemisphere.

Abscess 1 measured 45 mm. by 20 mm., with a connective tissue lining 1 mm. thick, and involved only the white matter Abscess 2 measured 6 mm. by 9 mm. by 5 mm., giving on cross section a type of diamond shaped cavity, lined by a connective tissue capsule 1 mm. thick, and involved both the white and gray substance. Abscess 3 measured 57 mm. by 41 mm. by 1 mm. in width (due to collapsed condition caused by evacuation of pus during removal), and involved the gray substance in the region of the motor area. Abscess 4 measured 9 mm. by 5 mm., with connective tissue capsule 0.5 mm. thick, and involved only the white substance.

Microscopical sections of the walls, stained by the hematoxylin-eosin method, showed four main types of cells. Polymorphonuclear cells in all stages of degeneration were the predominating type. Plasma cells, variable in size and with the large type predominating, were found chiefly in the periphery of the inflammatory area; a few near the pus zone, however. Large, round, vacuolated mononuclear wandering cells were found both within and without the pus zone. Fibroblasts were seen in all parts of the inflammatory area. An extremely thick exudate of fibrin was seen in all sections. Necrosis was evident in two instances. Perivascular infiltration and vascular distention were prominent.

Only two abscesses involved the gray substance: abscess 3, which had encroached on the motor area, and possibly caused spasticity of the right extremities, and abscess 2, which appeared to involve the auditory center, although no record of defective hearing is in the clinical history. The rest of the paths involved were the association, commissural and projection tracts.

Green, foul smelling pus exuded from the brain on section. A Gram stained smear gave a Gram-positive diplococcus and short chain coccus, and a Gram-negative bacillus with sharp-pointed ends (*B. fusiformis*). Cultivated under anaerobic conditions gave Gram-staining cocci and Gram-negative bacilli. Neither organism was found on anaerobic growth.

A bloody, mucoid exudate was obtained from the bronchiectatic cavity. A Gram-stained smear gave Gram-positive cocci in chain formation and Gram-negative bacilli. Cultured anaerobically gave Gram-staining cocci and Gram-negative bacilli (*B. fusiformis*). Aerobic conditions gave neither organism.

Kyphoscoliosis was present from the tenth dorsal to second lumbar vertebrae. (The etiology is apparently due to the "broken back," sustained fourteen years previous.) This

curvature left a cavity containing wedged-in lung and pleura, and it was in this pocket that bronchiectasis developed. Here the anaerobes, *B. fusiformis* and anaerobic streptococci, grew, there being little chance for drainage. Presumably, thence through the blood stream to localization in the brain, causing multiple abscesses. I have been unable to find any report in the literature of brain abscess occurring secondary to kyphoscoliosis.

The organisms isolated from the pus of the brain and lung were, without doubt, the same, *B. fusiformis.*

As to pathogenesis, it is easily seen that the conditions were ideal for anaerobic growth in the bronchiectatic part of the right lung. Most authors agree that commonly various organisms are transmitted through the blood stream or lymphatics to the brain. As most frequent invaders they place the pneumococcus, tubercle bacillus, staphylococci and streptococci and *B. fusiformis* as a rarer invader. *B. fusiformis* is found occurring in the mouth, beneath the gums, around carious teeth, in tonsils both diseased and normal, Vincent's angina, noma, etc. It lives in symbiosis with streptococci and spirilla in the actinomyces-like granules found in tonsillar crypts.

It would seem reasonable to assume that the fusiform bacilli and cocci, found in these various localities, passed down the trachea and bronchi into the bronchiectatic cavities where they caused suppuration and later by the hematogenous route localized in the brain causing brain abscesses.

SUMMARY

A case of multiple bilateral brain abscess, secondary to bronchiectasis caused by a wedging of the lower lobe of the right lung into a pocket formed by kyphoscoliosis is described.

The causative agents isolated and cultivated from both the abscesses and the suppurating lung were the *B. fusiformis* and anaerobic streptococci.

The most probable route by which the infection traveled from its primary focus was the blood stream.

Nov. 10, 1919.

OBSERVATIONS ON A GREEN-PRODUCING COCCUS FROM THE BRAIN IN A CASE OF ENCEPHALITIS *

S. JOHN HOUSE, M.D.
CHICAGO

I wish to report the results of the bacteriologic examination in a case of encephalitis, diagnosed clinically as encephalitis lethargica.

The case was that of a woman, aged 70, who entered the Cook County Hospital, service of Dr. J. A. Wolfer, March 5, 1919, with impaired mentality, apparently complete loss of memory, and a broken forearm. The present illness was said to have come on suddenly one morning three weeks previously with dizziness. Following this came mental changes that grew progressively worse. The forearm was broken while preparing her for the trip to the hospital. In the hospital, in addition to these changes, arteriosclerosis was found with increased knee jerk. She lived twelve days in the hospital. There was little or no fever (axillary) until the eighth day, when the temperature rose to 100 F., and also a few hours before death, when there was a sudden rise to 105 F. The respirations ranged between 19 and 22, rising to 38 five hours and dropping to 12 one hour before death. The pulse was about 80 most of the time, increasing in proportion to the temperature. She had no control over the bladder. She slept a great deal of the time and when not sleeping was stuporous and talked at random. Nothing abnormal was found in the urine except a few white cells on one occasion. The white blood cell count on three examinations at two-day intervals was 8,800, 9,400 and 12,000. No Wassermann, Lange or Nonne tests were made. The duration of illness was five weeks.

Anatomic Diagnosis (Dr. E. R. LeCount).—Encephalitis (lethargic type?); congestion and edema of the leptomeninges; hemorrhages in the trachea and lungs; hyperplasia of the tracheobronchial lymph glands; foramen magnum pressure furrow of the brain stem; marked general anemia; Colles' fracture of the left arm; petechial hemorrhages of the lining of the stomach, trigone, and rectum; senile arteriosclerosis; chronic diffuse nephritis; atrophy of the cerebral cortex; fibrous perivascular leptomeningitis with scars; external fibrous pachymeningitis.

* From the John McCormick Institute for Infectious Diseases.

Sections for microscopic study were taken from cortex of frontal and parietal lobes, lenticular nucleus and internal capsule, thalamus and hypothalamus, cerebral peduncles, pons, and medulla, and stained by the toluidin blue, Gram-Weigert, and hematoxylin-eosin methods.

An encephalitis was present, characterized in the cortex by an increase in glia cells, neuronophagia, a shrinkage of the nerve cells in their lacunae and a marked reticulation of neuroglia tissue. These changes were present in other sections also but to a less marked degree. There was a small amount of perivascular infiltration in some sections. Many of the small venous channels were greatly congested; no hemorrhages or typical plasma cells were seen. There was no evidence anywhere of thrombosis of the cerebral vessels.

In the sections stained by the Gram-Weigert method a few large diplococci and ovoid forms, similar in size and shape to those isolated and studied in pure culture, were seen. There was no regularity in their association with the pathologic changes, as they occurred both in the interstitial tissue and in relation to the cells showing neuronophagia.

Material was taken from the brain for cultures eleven hours after death. This material was obtained by means of sterile capillary pipets which were plunged into the brain at places seared by a red-hot spatula. The sites selected for this were the insula, the cerebral peduncle (about 0.5 to 1 cm. proximal to the pons), and along the inferior lateral border of the temporal lobe. The direction and depth of insertion of the pipets were gaged by sections of a brain hardened in formaldehyd. Then by a few short jabbing motions, with suction at the same time, brain material was drawn into the pipettes and transferred to tubes of melted agar (10 c.c.), kept at 46 C., to which goat blood had been added (10 drops to the tube). The material was emulsified against the sides of the tubes, appropriate dilutions made and plates poured in the usual way. These were incubated for twenty-four hours and studied. A diplococcus grew in pure culture. Not one of the uninoculated plates yielded any growth.

The cerebrospinal fluid and heart blood obtained postmortem were sterile.

The diplococcus stains by Gram's method: The individual cocci vary in size from about 0.25 to 0.75 micron in diameter, the greatest variation being seen in the short chains which contain from four to eight elements. The diplococcic forms, although similar in shape, differ markedly in size. There are also a few large ovoid forms, 0.75 to 1.25 microns in diameter, which occur singly. All these variations are to be found in a twenty-four hour blood-agar culture.

On blood-agar plates, after twenty-four hours' incubation, pin-point colonies are formed, surrounded by a 0.5 mm. greenish zone; the surface colonies are larger, 0.5 to 1 mm. in diameter, greenish, and have a greenish zone about them; they are round, moist, and slightly convex. After seventy-two hours there is a small amount of true hemolysis around the colonies. In plain broth a smooth cloudy suspension is formed with some fine white sediment which is readily diffusible. On plain agar a moderate growth occurs which is moist and slightly opaque to reflected light. On blood serum the organism grows rapidly. Litmus milk is made slightly acid. Using a 1 per cent. solution of the various sugars in sheep-serum water, with litmus as the indicator, lactose, mannite, salicin, dextrose, and saccharose were fermented; inulin was not. The final readings were made after seventy-two hours.

Rabbits and guinea-pigs were injected by various routes, including the intracerebral, with a thick suspension of twenty-four hour cultures of the diplococcus recovered from the brain, but all remained well except one rabbit that died sixteen days after the injection, apparently from some other cause.

Normal rabbits were injected intravenously at weekly intervals with suspensions of this organism, heated at 56 C. for thirty minutes. The suspensions were made from blood-agar slants, the initial dose being one slant. After repeated injections, serum was drawn and its agglutinins and opsonins studied. In both the agglutination and opsonic tests, twenty-four hour dextrose broth cultures were used with normal rabbit serum and salt solution controls. The agglutination mixtures were incubated at 37 C. for two hours, placed at room temperature for eighteen, and the final readings made. In the opsonic tests, fresh normal human leukocytes were used, and the final mixtures (diluted serum, leukocytes and dextrose broth suspension) were incubated at 37 C. for thirty minutes, smears made on slides and the point of opsonic extinction determined.

The results shown in the table indicate that immunologically the coccus isolated is distinct from similar green-producing cocci from poliomyelitis, influenza and other sources.

It is of special interest that von Wiesner,[1] the only observer that so far as I know has reported the results of bacteriologic studies of cases of lethargic encephalitis, recovered a gram-positive diplococcus from the brain of every case which he examined (he does not

1. Von Wiesner: Wien. klin. Wchnschr., July 26, 1917; quoted by Wilson, S. A. K.: Lancet **2**:7 (July 6) 1918.

say how many). He does not state that he found the organism in the microscopic preparations.

It is to be noted that the type of changes in this brain are essentially the same as those described by Bassoe and Hassin[2] in their report of three cases, the chief difference being one of degree. It is also interesting to note that a careful review of the reported cases of lethargic encephalitis has failed to reveal any uniformity in the degree in which these changes may occur in the various portions of the central nervous system; nor is there any definite grouping of pathologic changes that can be described as occurring in all of the reported cases.

REACTIONS OF SERUM OF RABBIT INJECTED WITH ENCEPHALITIC COCCUS

Strains of Cocci	Agglutination	Opsonic Extinction
Encephalitic coccus used for immunization	50,000	6,400
Poliomyelitic coccus	800	150
Poliomyelitic coccus	100	75
Poliomyelitic coccus	400	300
Green producing streptococci from influenza:		
Brain	1,600	1,200
Brain	1,600	150
Brain	1,600	75
Brain	1,600	6
Lung	1,600	300
Lung	1,600	35
Sputum	1,600	15
Lung	400	0
Cerebrospinal fluid	200	35
Pneumonia	200	6
Cerebrospinal fluid	100	15
Blood	100	15
Sputum	50	0
Lung	50	0
Cerebrospinal fluid	50	35
Blood	0	0
Sputum	4	15
Several strains of green producing cocci from measles and rubella	0	0

With normal rabbit serum the encephalitic coccus was agglutinated at a dilution of 20 only; practically no phagocytosis.

The fact that the heart blood and cerebrospinal fluid were sterile indicates that the infection of the brain was not agonal.

The diplococcus isolated is a large green-producing streptococcus, similar in many respects to other green-producing cocci, but apparently different in its immunologic reactions.

Nov. 10, 1919.

2. Bassoe and Hassin: Arch. of Neurol. and Psych., 2: 24, 1919.

RETROPERITONEAL LIPOSARCOMA

REPORT OF AN UNUSUALLY LARGE SPECIMEN WITH CHEMICAL ANALYSIS *

EDWIN F. HIRSCH AND H. GIDEON WELLS

This report consisted of a study of a case of edematous fibro liposarcoma without myxomatous elements, occurring in the retroperitoneal tissues and weighing 69 pounds, this being the largest solid tumor of which record could be found in the literature. With the naked eye a considerable portion of the tumor seemed to be fatty tissue although mostly it was edematous fibrous tissue. Microscopically, it varied from pure fatty areolar tissue to sarcoma tissue with abundant extremely atypical cells. Analysis of the tumor showed the presence of 90.53 per cent. of water, no appreciable mucin, nearly 3 per cent. of fat and 6.5 per cent. protein, so that about one third of the dry weight was fat. Outside the tumor the body showed the most extreme possible degree of emaciation and fat absorption, although the tumor had nevertheless accumulated nearly 2 pounds of fatty material and 4½ pounds of protein. It illustrates the capacity of a malignant tumor to retain large amounts of fat under conditions in which the normal fat deposits give up all their fat.

Nov. 10, 1919.

* Full report will be published in the *American Journal of Medical Sciences.*

PRIMARY SPONTANEOUS TUMORS OF THE OVARY IN MICE*

MAUD SLYE, HARRIET F. HOLMES
AND
H. GIDEON WELLS

From the Otho S. A. Sprague Memorial Institute and the Department of Pathology of the University of Chicago

Among 22,000 mice of the Slye stock dying natural deaths at all ages were forty-four mice with spontaneous primary ovarian tumors, not including simple ovarian cysts. Of these, thirty-eight had simple benign solid papillary adenomas, only occasionally with slight cyst formation. One showed a typical papillary cystoma. One had a typical solid teratoma containing a great diversity of tissue elements. Of the thirty-eight cases of solid papillary adenomas, nineteen, or 50 per cent., were bilateral, so that there were fifty-seven tumors of this class. There were four unquestionable primary malignant tumors of the ovary, all showing the "mesothelioma" type of growth characteristic of malignant tumors derived from the sex glands; one of these produced perirenal metastases. There was one other tumor of the same type primary in either the ovary or the adrenal. Two round cell sarcomas were found that arose either from the ovary or some other organ, while two other sarcomas had produced secondary growths in the ovary. Of the forty-four mice with primary ovarian tumors, twenty-six had tumors in other parts of the body.

In the literature were found reports of eight other cases of tumors arising in the ovaries of mice, which exhibited quite the same characteristics as the tumors described in this paper.

Dec. 8, 1919.

* Full report will be published in the *Journal of Cancer Research.*

MARKED BLOOD CHANGES ACCOMPANYING LYMPHOSARCOMA

EDWIN F. HIRSCH

From the Laboratories of the Camp Grant Base Hospital and St. Luke's Hospital, Chicago

Changes in the blood of patients with a malignant tumor are usual, the commonest of which are disturbances in erythropoesis. There may be a mild or severe anemia, in the latter instance accompanied by anisocytosis, poikilocytosis, polychromatophilia, or other degenerative changes of the red cells, and the appearance of normoblasts in the peripheral circulation. The number, variety, and ratio of leukocytes

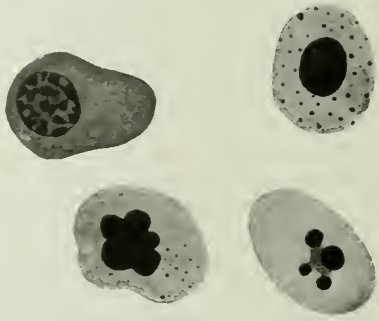

Fig. 1.—Sketch illustrating the various kinds of nucleated red cells.

may deviate from the normal. These changes vary both with the particular tumor, and the response of the patient's tissues to the tumor growth. The location, the growth power, the tissues into which metastases occur, and such added factors as necrosis, secondary infection, and hemorrhage exert an important influence on the alteration of the blood. Naegeli[1] describes many such changes accompanying malignant tumors, and records an extensive bibliography.

Still other blood changes usually accompany invasion of bone tissue, such metastases being observed

1. Naegeli, O.: Blutkrankheiten und Blutdiagnostik, Leipzig, 1912.

more frequently perhaps with carcinoma, but also with other malignant tumors. Their exact nature may not be stated definitely, although nucleated red cells, immature leukocytes, or their bone marrow antecedents are commonly found in stained blood films. Alterations of this kind accompanied by those of a severe anemia become important in the presence of a limited tumor growth where acute or chronic myelogenous leukemia, pernicious anemia, or other diseases with severe blood disturbances are being considered.

The unusual changes in the blood of a patient at the Camp Grant Base Hospital with an abdominal lymphosarcoma and its rapidly fatal course prompted the preparation of this report. Mackenzie[2] reported a

Fig. 2.—Sketches illustrating the red cell changes.

study of four patients with lymphosarcoma, and in summarizing the literature noted the distinction between such tumors whose growth remains regional, and those with widespread secondary metastases. Blood examinations of one in the first mentioned variety disclosed a leukocytosis of 14,000 to 25,000 and in twenty-eight days the percentage of hemoglobin changed from 90 to 5. The polynuclear leukocytes and lymphocytes respectively constituted 70 to 78 per cent. and 26 to 30 per cent. of the total. Blood examinations of the two patients with widespread metastases are recorded without special changes, although with one small metastatic nodules were found postmortem in the femur.

2. Mackenzie, George M.: Cases of Typical and Atypical Lymphosarcoma, J. Cancer Research **3**: 93-106, 1918.

According to Ewing,[3] anemia and cachexia develop early, while an increase in the number of leukocytes is common and may be so marked as to suggest leukemia. Other authors quoted by Ewing state that the excess is usually of the polynuclear leukocytes, occasionally of lymphocytes, and rarely of eosinophil cells, while atypical cells found in the tumor may appear in the blood stream in such numbers as to suggest leukemia. In fact, he continues, the distinctions between lymphosarcoma and leukemia cannot always be drawn sharply. Probably the most extensive report on lymphosarcoma in this country is by MacCallum.[4] He records studies on eight, three of them intrathoracic, the others abdom-

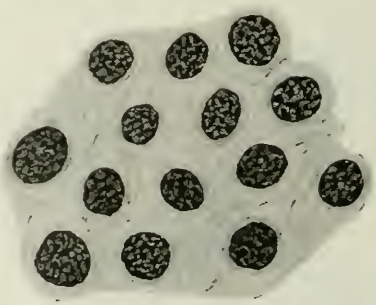

Fig. 3.—High power drawing representing the tumor cells and their arrangement.

inal. These tumors correspond closely with the description given by Kundrat. MacCallum states that there may or may not be alterations in the blood, depending upon changes in the hemopoietic tissues. Where blood examinations are recorded for his patients reduction of the red cells and hemoglobin was the commonest. The white cells were normal or only slightly increased in number excepting with one where a marked leukocytosis (lymphocytes predominating) is given; 1.4 per cent. of the white cells in another with

3. Ewing, James: Neoplastic Diseases, 1919, p. 366.

4. MacCallum, W. C.: On the Pathological Anatomy of Multiple Lymphosarcoma and its Status with Relation to Hodgkins Disease, Trans. Assn. Am. Phys., 1907, pp. 220, 350.

bone marrow metastases are recorded as myelocytes, and 14.9 per cent. as large mononuclear. Polynuclear leukocytes predominated in the differential counts with the others.

Clinical History.—The patient, a soldier, 21 years of age, American born, after ten months' service was admitted to the Camp Grant base hospital, stating that three weeks before he noticed a dull, aching pain in the lumbar region of his back, which extended into the pelvis and hips, and became severe a few days before admission. He was symmetrically developed, of fair nourishment, having a pale skin, loosely adherent to the underlying tissues. The pupil reflexes were active, the sclerae pale, and beneath the conjunctivae were a few recent petechial hemorrhages. The tongue was dry, coated and blood oozed from the gum margin about the left upper cuspid tooth.

CHART 1.—URINE EXAMINATIONS

Day in Hospital	Volume in 24 Hours, C.c.	Albumin	Blood
1	.....	0	....
2	.....	0	....
3	.....	..	....
4	.....	+	++
5	.....	+	++
6	.....	..	....
7	.....	+	++
8*	270	+	++
9	150	+	++
10	2,600	+	+
11	4,200	+	+
12	3,250	+	+
13	2,700	+	+
14	2,000	+	+
15	2,900	+	+
16	1,400	+	+

* From 8th to 16th day, inclusive, hyaline and granular casts, many leukocytes.

The skin of many parts of the body contained numerous petechial and larger hemorrhages, both recent and disappearing. There was a slight pitting edema of the ankles. The superficial epigastric veins, especially the right, were prominent, suggesting obstruction to the venous circulation of the lower extremities. The lungs were resonant, the breath sounds clear, the heart borders normal. The abdomen was distended, tympanitic, and patient complained of severe pain in the lumbar region of the spine, especially on deep palpation in the left kidney region, where an indefinite mass about the size of a goose-egg could be felt at the kidney level. The

TABLE 2

	Day in Hospital										
	5th	7th	8th	9th	10th	11th	12th	13th	14th	15th	16th
Leukocytes	15,600	13,500	15,900	14,700	14,500	12,400	11,400	11,400	13,200	16,200	21,000
Red cells	4,500,000	3,100,000	2,600,000	.....	2,000,000	1,500,000	1,600,000	1,100,000	980,000	600,000	700,000
Hemoglobin	.....	60%	50-60%	.....	50-60%	40-50%	40-50%	40%	30-40%	20-50%	30%
Color index	.....	1+	1+	.....	1+	1+	1+	1+	1+	1+	1+
Small lymphocytes	.....	38	42	.....	40	40	41	41	.....	.....	42
Large lymphocytes	.....	12	10	.....	12	9	8	6	.....	.....	6
Mononuclears	.....	2	2	.....	0	0	1	1	.....	.....	1
Polymorphonuclear											
Eosinophils	.....	2	1	.....	1	1	2	1	.....	.....	1
Neutrophils	.....	37	39	.....	36	41	41	39	.....	.....	44
Basophils	.....	1	1	.....	1	1	1	1	.....	.....	0
Transitionals	.....	4	4	.....	5	4	4	4	.....	.....	5
Myelocytes											
Eosinophils	.....	1	0	.....	0	1	0	1	.....	.....	0
Neutrophils	.....	3	1	.....	4	3	2	5	.....	.....	1
Basophils	.....	0	0	.....	0	0	0	1	.....	.....	0
Tüek irritation forms	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	1
Anisocytosis	.....	.....	.....	.....	.....	+	+	++	.....	++	++
Poikilocytosis	.....	.....	.....	.....	.....	.....	.....	+	.....	+	+
Basophilic granulation	.....	.....	+	.....	+	+	+	+	.....	++	++
Nucleated red cells	.....	++	++	.....	++	+	++	+++	.....	+++	+++
Megaloblasts	.....	.....	.....	.....	.....	.....	+	+	.....	+	+
Cabot's ring bodies	.....	.....	.....	.....	.....	.....	.....	.....	.....	+	+

pain elicited by palpation radiated into the urinary bladder and to the head of the penis. The spleen was palpable below the costal arch the breadth of three fingers. All of the usually tested reflexes were present and reacted normally. The urine examined on the fourth day after admission was bright red with blood. Urine examinations made repeatedly during the soldier's illness in the hospital are recorded in Table 1. The leukocytes constantly were increased above the normal number, and stained blood films contained numerous nucleated red cells, myelocytes, megaloblasts, and in the later states of the disease, when the anemia had become severe, red cells irregular in size and shape, some of them containing Cabot's "ring bodies" and basophil granules. The results of the blood examinations are recorded in Table 2. A blood culture was negative. Severe hemorrhages from the nose, and almost constant oozing of blood from the gum margins were added features of the clinical course. The soldier gradually became weaker and died on the seventeenth day after admission.

Clinically, a final diagnosis was never made with complete satisfaction. A malignant tumor of the urogenital passages with bone metastases was considered seriously, but acute myelogenous leukemia was never definitely excluded, and in fact this was largely favored because of the blood alterations. Postmortem examination disclosed the presence of a lymphosarcoma of the abdomen.

Postmortem Examination.—The body is that of an adult white man, with a marked palor, 173 cm. long, and weighing about 140 pounds. The sclerae are pale, the cotton removed from the nostrils is stained red with blood, and along the gum margins of the teeth there is a little blood. There are numerous recent and disappearing hemorrhages, petechial to 1 cm. in size in the skin of the trunk and extremities, while on both arms there are extensive suggillations about venae puncture wounds. There is a pitting edema of both ankles, and the superficial epigastric veins are moderately distended.

The skeletal muscles are pale, and in the root of the mesentery there is a hemorrhage fully 15 cm. in its maximum dimensions. Under the visceral pericardium, there are numerous petechial hemorrhages. In the examination of the heart only a palor of the myocardium is noted. Beneath the pleura of each lung are pink discolorations, ½ cm. in diameter, and also petechial hemorrhages. There is no inflammatory consolidation of the lungs, nor do they contain tumor metastases.

On eviscerating the chest and abdomen in the usual way, there are white nodular masses in the lower thoracic region closely adherent to the anterior surface of the vertebral bodies. They are intimately associated with and in the lymph glands, forming in the lower thoracic region a mass 14 by 9 by 2 cm., the upper level of which is opposite the ninth ribs, the lower level opposite the third lumbar vertebra. This mass of tissue merges imperceptibly into another lying on the floor of the pelvis 8 by 4 by 3 cm., with extensions to the right and left groins, respectively, 11 by 5 by 4 cm. and 12 by 7 by 2½ cm. Those nodes in front of the spine extend down to the vertebral surfaces, and on the fifth lumbar there

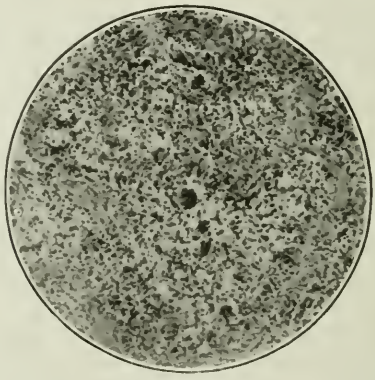

Fig. 4.—Low power photomicrograph of the lymphosarcoma.

is an erosion about 2 cm. in diameter, very superficial. All of the tumor nodules varying in size up to the confluent masses mentioned are pale white and firm, excepting in the pelvis, where areas of bright red or brown are mottled against the white. The entire outline of the prostate is lost, and there is both constriction and erosion of the pelvic portions of the ureters. The urinary bladder is also invaded, its mucous surface containing hemorrhages, 0.5 to 1.5 cm. in diameter. At the bifurcation of the inferior vena cava into the right and left iliac veins, these branches and their ramifications are constricted, and coarse nodules project into their lumina. There is no ulceration of the rectum, but opposite the prostate its lining is puckered over an area 0.5 cm. in

diameter. There are no changes of the brain other than an anemia, and the bone marrow of the calvarium and ribs is not increased.

Histology.—Sections of the white nodular tissue contain tumor cells repeating the structure of a lymphocyte, but slightly larger. Between the individual cells is a delicate fibrous tissue stroma. The cells are arranged in cords and alveoli, ¼ to 1 mm. in diameter. Many such alveoli are tumor cells closely crowded together, others appear as clear spaces lined by a single layer of tumor cells, with a few lying in the space. Septa of fibrous tissue limit the alveoli of cells. Where the tissue is dense the tumor cells are crowded and appear polygonal or slightly spindle-shaped. In sections from the pelvic mass necrosis and large hemorrhages are common. Hyalin masses containing nuclear fragments and appearing like Langhans giant cells are frequent in the necrotic alveoli.

Kundrat[5] in 1893 clearly differentiated the lymphosarcoma from other malignant tumors.[6] He described them as neoplasms arising only from groups of lymph nodes, not from single nodes, and from adenoid tissue of the mucous membranes. Extension into the surrounding tissues occurs from these points and secondary tumors appear almost exclusively in the intestinal mucosa, serous membranes, and lymph nodes. These are not spontaneous atypical growths, but are masses of tumor tissue joined to the primary tumor by continuity through the lymph channels. The location of secondary tumors and their union by continuous growth through the lymph channels are features differentiating lymphosarcoma from other sarcomas and carcinoma.

The lymphosarcoma described in this report belongs to the variety described by Kundrat. Its rapid clinical course with marked changes in the blood give it a peculiar interest. Although a tumor of this kind is not likely to reach the dimensions noted at postmortem within a period of five weeks, symptoms suggesting its

5. Kundrat: Wiener klin. Wochschr. **6**: 211-12, 234-239, ,1893.
6. See articles by Fraenkel, E., and Sternberg, Carl, on Pseudoleukemia, and subsequent discussions by others in Verhanlung der Deutsch. Path. Gesellsch. 15 Tagung 1912, 1 and 11 Sitzungen.

presence were not noted before that time by the patient. The blood changes occurred rapidly during the seventeen days the soldier was in the hospital, but even the initial blood examinations disclosed nucleated red cells and immature bone marrow cells. Lymphocytes in the differential examinations constituted 48 to 52 per cent. of the leukocytes. With the increasing anemia, changes in the size, shape, and appearance of the red cells were noted in the blood films. Repeated hemorrhages from the urinary passages, the nose, mouth, and other tissues no doubt were influencing factors in the rapidly progressing anemia. To what extent erosion of the vertebral column influenced the blood picture is problematic, but it seems likely that bone irritation of some kind was present to provoke some of the changes.

A tumor of this kind pursuing a rapidly fatal course with severe disturbances of the blood deserves consideration because of the confusion likely to result in differentiating a number of severe primary or secondary blood diseases, particularly those anemias and leukemias without clear cut characteristics. Malignant tumors accompanied by blood changes of this kind form another group of diseases that must be considered in a differential diagnosis.

SUMMARY

An abdominal lymphosarcoma with marked blood changes and an unusually rapid fatal course is described. The blood changes accompanying its growth are such as might readily be confused with those of a leukemia, or a severe primary anemia.

Jan. 12, 1920.

FACTORS INFLUENCING THE FINAL HYDROGEN-ION CONCENTRATION IN BACTERIAL CULTURES

WITH SPECIAL REFERENCE TO THE STREPTOCOCCI

HORRY JONES

From The Department of Pathology and Bacteriology, University of Illinois, College of Medicine, Chicago, Ill.

The final hydrogen-ion concentration of virulent streptococci varies with different strains between p_H 4.8 and 5.4; of non-virulent streptococci between 4.2 and 4.7; of pneumococci between 5 and 5.6 for the limited number of strains studied.

The regularity with which a given strain can reproduce its final hydrogen-ion concentration under favorable and constant conditions is striking. This concentration, however, is not independent of the initial p_H of the medium, or of its composition, etc., as has been claimed by some. In fact, the initial reaction of the medium, even though growth does occur, is a most important factor in causing irregularities in the determination of this particular characteristic.

Temperature at which the culture is incubated, age of the culture from which the inoculation is made, variety of fermentable carbohydrate used, buffer content of the medium, are a few of the common causes of wide variations in the final hydrogen-ion concentration of a given strain.

However, it is perhaps true that with a given carbohydrate in excess of the amount used by the organism, and with conditions favoring a rich growth of the culture, the limiting hydrogen-ion concentration for a given strain will be reproducible and characteristic, and therefore of diagnostic value.

The addition of blood, serum or ascitic fluid to the medium in very small amounts in some way increases the tolerance of the pneumococcus and streptococcus to the toxicity of the hydrogen-ion. Because of this,

final concentrations are then produced, imitating those concentrations reached by streptococci of avirulent types, and thus confusing the three varieties.

No explanation of the mechanism by which these body fluids increase the tolerance of the organism to hydrogen-ion is here attempted. Strong acidification, long boiling, etc., completely destroy the mechanism of this unknown "active principle." Further search may reveal still other phenomena having "vitamins" as a basis of their explanation.

Jan. 12, 1920.

TRANSACTIONS OF THE CHICAGO PATHOLOGICAL SOCIETY

VOL. XI. JUNE 1, 1920. NO. 3

TUMORS OF THE HYPOPHYSIS

AN EPITHELIAL INFUNDIBULAR TUMOR; ADENOMATOUS HYPERTROPHY OF THE HYPOPHYSIS WITH HEMORRHAGE AND RUPTURE THROUGH THE NASOPHARYNX; HYPOPHYSEAL CYST *

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When P. Marie and Marinesco published their memoir on acromegaly in 1891 a great impetus was given to the investigation of hypophyseal function with its disturbances, and the literature is now voluminous.†

Although the reports on pituitary hypertrophy have added greatly to our knowledge of hypophyseal function, much remains for investigation. The three hypophyseal lesions in this report are interesting because of the few symptoms they caused.

CASE 1.—A Polish laborer, 28 years old, was brought to the Cook County Hospital on Jan. 20, 1918, to the service of Dr. Goldsmith where a diagnosis of cerebral tumor with hemorrhage and possible lues was made. On entrance he was in coma. His wife said fifteen hours previously he awoke at 3 a. m. with an intense headache and pain in the back; these persisted and about nine hours later he vomited, and three hours later became unconscious. This sudden onset had been

* For literature consult the following:

Cushing, Harvey: The pituitary body and its disorders; clinical states produced by disorder of the hypophysis cerebri; Philadelphia and London, 1912, J. B. Lippincott Co.; 351 pages.

Erdheim, J.: Ueber Hypophysenganggeschwülste und Hirnscholesteatome. Sitzungsberichte der Kaiserlichen Akademie der Wissenschaften in Wien. December, 1904, Vol. CXIII.

Presbeanu, Nicolas: De l'hypophyse dans l'acromegalie. Thèse pour le Doctorat en Medecine, Paris, 1909.

The Hypophysopathies. Monographic Medicine, New York and London. D. Appleton Co., 1917, IV, pp. 912-932.

preceded by several months of weakness and occasional headaches during which he had not worked at his occupation, tin plater.

In the hospital the limbs were spastic with frequent clonic seizures at intervals of five to ten minutes; these appeared first in the right then in the left arm, lasting about a minute; the right eye deviated to the right and the pupil was larger than the left, the reaction to light was absent and there was slight nystagmus of the right eye; patellar reflexes were exaggerated; Babinski's sign positive; cremasteric reflex absent; ophthalmoscopic examination negative. There were periods of apnea, followed by slow, shallow breathing, each lasting five minutes; systolic blood pressure, 120; leukocyte count, 9,100; pulse, 50; respiration, 18; temperature, 97 F.; involuntary urination; spinal fluid clear with no increased pressure; butyric acid and Nonne tests positive. In spite of stimulating treatment death occurred after fourteen hours.

Necropsy (Dr. E. R. LeCount): Only such details are mentioned as have a bearing on the subject. This is the body of a white man, 174 cm. long, weight 108 pounds, with light brown scalp hair, dark brown eyebrows, small ears and nose and a light brown mustache; body nourishment is poor, muscular development slight; the feet large; bones of extremities long and thin; axillary hair absent and pubic hair very scanty; the calvarium thin yellow bone; the brain with cerebrospinal fluid 1,560 gm.

The thyroid gland weighs 50 gm.; it is in all essentials normal grossly. The thyroid and costal cartillages are soft. The cervical lymph glands are large; some of them 2 cm. in diameter. The suprarenal glands weigh together 12 gm., they are very small; the cortices are very thin but light yellow. The spleen weighs 160 gm. The surfaces made by sectioning the pancreas are normally pink and grossly unaltered. The testes are very small. There is no change in epididymides; the prostate is small. The lymph glands of the mesentery of the small bowels are large, bright red, the largest about 2 cm.

In removing the brain in the usual manner, there is exposed a firm, gray mass projecting from the sella turcica into the base of the brain, just behind the optic chiasma. This is removed with the hypophysis to which it is attached. The sella turcica is very flat, 27 mm. wide and 20 mm. front to back. On the dorsum sellae there is a sharp ridge longitudinally in the center and gently sloping on both sides. The brain after ten days in formalin (10 per cent.) has flat cerebral convolutions; the vessels of the leptomeninges are filled with dark-red blood and the fine arterioles stand out sharply.

In the pia-arachnoid, of both the frontal lobes and the right superior parietal gyrus there are patches of petechial hemorrhages 2 to 4 cm. in size; along some of the larger vessels the leptomeninges are opaque and all over the brain lifted by fluid. The arteries at the base of the brain are normal. The hemispheres at the base are normal, but near the chiasma opticum and involving it, there is a growth continuous with the infundibulum; the tuber cinereum, infundibulum and the corpora mamillarae are completely obliterated by it, only the front margin of the optic chiasma and the optic nerves appear unchanged. The base of the left cerebral peduncle is considerably depressed, so is the front of the pons which is also

Fig. 1.—Coronal section through the third ventricle, one-half the normal size (water-color drawing). Honey-combed tumor filling the third ventricle. Throughout the tumor are multiple cysts, separated by thick septa, the whole bounded by a dense fibrous capsule.

sloping. Both the occulomotor nerves at their point of issue are flat and bandlike, especially the left. Surfaces made by sectioning the brain into coronal segments, 1 cm. thick, are peppered with large punctae vasculosae; the ventricles are enormously distended and the lateral ventricles are 2 cm. high and 2 cm. wide, at the anterior commissure; the third ventricle is completely filled and greatly enlarged by the tumor which is triangular in shape and 3.5 cm. at the base, which lies free between the hypocampal gyri. Its flattened apex presses against the fornix; this tumor is 4.2 cm. long and extends from the front of the chiasma to the posterior commissure; it is solidly connected with the chiasma and fuses into the surrounding tissue. Its middle and back parts are loose and surrounded by a dense, fibrous capsule and can

be easily lifted to expose the enormously distended third ventricle (see Fig. 1). The ependyma of all the ventricles is considerably thickened; in the lateral ventricles it is perforated by the tumor which bulges into both the ventricular cavities.

There are multiple, punctiform hemorrhages in the back part of the left thalamus, from 1 to 2 mm. in diameter. The choroid plexus in the inferior cornu contains many glistening globular bodies from 2 to 4 mm. in size.

The tumor is very granular and firm; inside it is mottled with light gray places which are separated by yellowish-green globular pearly masses. The septa, which gave a honey combed appearance, contain lime.

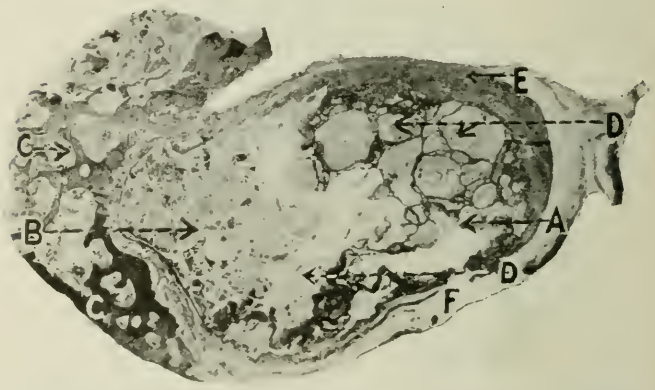

Fig. 2.—Photograph of a single section 20 by 19 mm. in diameter; from the center of the growth, A, anterior lobe; B, posterior lobe; C, fragments of cella turcica with infiltrated tumor tissue; D, cysts; E, solid strands of anterior lobe cells; F, dura mater (dia. 4).

The hypophysis, which was connected with the tumor by a small pedicle, is irregular in shape, grossly granular and weighs 1.6 gm.; its sagittal surfaces measure 19 by 15 mm.; it has a dense, grayish-brown, fibrous capsule.

Anatomic diagnosis: Tumor of the hypophysis; petechial hemorrhages in the leptomeninges; punctiform hemorrhages in the brain substance; edema of the brain and the leptomeninges; hyperemia of the brain and the leptomeninges; internal hydrocephalus; multiple cysts in the choroid plexus.

Histology (Serial sagittal sections): About two thirds of the hypophysis consist of large and small cysts, and spaces filled with blood, the rest is made up of strands of epithelial cells which branch and anastomose with each other. Solid epithelial masses are scattered in between. (See Fig. 2.)

The cysts are distinctly separated from the stroma by a membrana propria; they have linings of single and stratified columnar epithelium with long and dark staining nuclei; some are entirely filled with a homogeneous staining substance resembling coagulated plasma other epithelium less altered, fibrin and fatty acid crystals. In a few of these cysts hemorrhage has taken place.

The solid epithelial islands consist at the periphery of flat, irregular cells, very poor in protoplasm and dark staining nuclei; towards the center the cells become more cubical or round and have larger cell bodies with larger and paler nuclei. The appearance of these cell-nests varies according to the extent of the degenerative changes; there are islands with concentric masses of huge hyalin or necrotic spindle-shaped epithelial cells with a great amount of finely granular protoplasm and faintly staining vesicular nuclei (see Fig. IV. B); they are slightly compressed and laminated; some of these islands have undergone liquefaction necrosis and others have accumulated large amounts of lime salts and stand out as dark, structureless masses. Only a little tissue is found resembling normal tissue of the hypophysis; it is seen at the periphery of the anterior lobe consisting of twenty to thirty columns of apparently normal gland cells with a small amount of cytoplasm and small, round, dark-staining nuclei (Fig. IV. A); their cell-body is not well defined and their structural characteristic and staining properties are that of chief-cells or so-called neutrophiles (chromophobes), toward the center these columns are interspersed by a few cells with large protoplasm staining more intensely with eosin.

Adjoining the posterior lobe and only separated by the dense large fibrous capsule which envelopes the whole growth are seen multiple bony lamellae (fragments of the sella turcica), containing circular cavities in which are lymphocytes, erythrocytes, and cells resembling the chromophobe cells and altogether giving the appearance of bone marrow. (Fig. 2. C.)

The tumor mass which is embedded in the third ventricle is histologically exactly the same as that below only that the retrogressive changes are more pronounced. There is a complete absence of hypophyseal cells. (Fig. 5.)

Diagnosis: Infundibular epithelial tumor of the hypophysis with cysts (Erdheim type).

Remarks: The length of the extremities and large feet would indicate hyperfunction, which later was followed by dystrophy; but the length of the extremities may also be ascribed to the atrophy of the genital

glands before puberty (Brown-Séquard) and here we find that the testes were very small.

Large feet, if not abnormally so, are found in many people without special disturbances of internal secretion. Absent axillary hair and scanty pubic hair and

Fig. 3.—Photomicrograph of a section with large cysts and at A, solid masses of epithelium; B, large and small cysts in pars anterior (dia. 100).

soft costal cartilage may be regarded as a consequence of glandular dystrophy, perhaps also the emaciation and slight muscular development; all other symptoms and signs can be accounted for by pressure of the base of the brain, giving rise to the so-called interpeduncular syndrome.

* L. c., p. 71-80. Case 1, figs. 11, 12, 13, 14 and 15.

In all essentials the growth in this case corresponds to one reported by Erdheim.*

Case 2.—A man, 57 years old, blacksmith, single, was brought to the hospital of the House of Correction to the service of Dr. Sceleth in coma and with a diagnosis of alcoholism. He had been drinking very heavily for three weeks. On examination the pupils were small and did not react to light; patellar reflexes were exaggerated and Babinski's sign was negative. He died a few hours after admission.

Necropsy (Dr. E. R. LeCount): This is the body of a white man, 164.5 cm. long; weight, 116.5 pounds; scalp hair absent in front and on sides, red-gray eyebrows, mustach, axillary and pubic hair; body nourishment and muscular development fair; the long bones medium size, the arms and legs well proportioned to the trunk.

The suprarenal glands seem small and are otherwise grossly unaltered. The heart is small and with 2.5 cm. of the aorta and 1 cm. of the pulmonary artery, weighs 220 gm. There is only one coronary artery. In the thymic body there is nothing but fat; the pancreas is normal size. In the head of the left epididymis there is a cyst 9 mm. in diameter containing clear fluid, it replaces most of the head. The testes are without gross change. The biliary lymph glands are small. The dura mater is pale, the cerebro-spinal fluid clear. In cutting the roots of the optic nerve, in the usual way, in removing the brain, the knife slips through the dura covering the top of the sella turcica and hypophysis and a transverse slit is cut without warning through the top of a cyst which apparently occupies all the body of the sphenoidal bone and the sella turcica; it is filled with about 15 c.c. of clear colorless fluid. The lining of the cavity is smooth; the infundibulum and the minute hypophysis are about the size of half a pea. The brain with the cerebrospinal fluid weighs 1,480 gm.

When hardened the brain is pale; the cerebral convolutions are flat; the sulci are broad and shallow; the vessels of the leptomeninges are partially empty; the leptomeninges are raised by turbid fluid; there are multiple grayish-yellow opacities 2 mm. in diameter in the leptomeninges of the sides of both frontal lobes. There is a slight foramen magnum pressure furrow of the brain stem and cerebellum; the arteries of the base of the brain are slightly thickened; surfaces of coronal segments are paler than normal; the punctae vasculosae not distinct.

The sella turcica is 24 mm. wide and 22 mm. front to back; its cavity is about 21 mm. deep at the center. On the frontal

side of this cavity lies the hypophysis about the size of a half pea; this is excised; it weighs 48 mg.

Anatomic diagnosis: Cyst of the hypophysis; edema and anemia of the brain and the leptomeninges; fibrous scars of the leptomeninges; slight sclerosis of the cerebral arteries.

Histology: In serial sections of the hypophysis very little of the frontal lobe is left, the tissue of the posterior lobe is

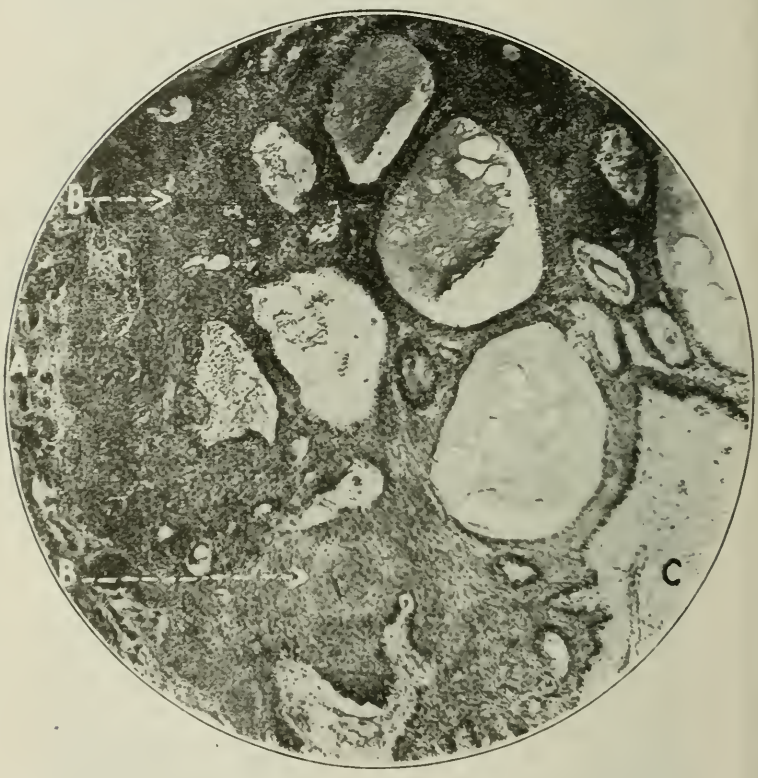

Fig. 4.—Photomicrograph; A, strands of anterior lobe cells at the margin; B, solid strands and masses of epithelial cells; C, cyst filled with hydropic cells (dia. 100).

normal except for minute engorged veins, most of the section being composed of the pars intermedia which is extremely vascular, much more so than either the pars nervosa or glandularis.

The remaining tissue of the anterior lobe is formed by columns of gland cells and acini, which latter contain a

small amount of colloid-like substance in their center, the gland cells are mostly of the chromophile type, acidophiles and basophiles. The acidophiles are slightly more numerous in some sections, from the center of the gland; while the basophiles predominate toward the periphery.

The cells lining the acini are large with very irregularly shaped, shrunken cytoplasm, which is faintly granular; their nuclei are also irregular in size and shape. There are between the acini wide trabeculae of fibrous connective tissue.

The cells of the pars intermedia have small, round, dark-staining nuclei with hardly any visible cytoplasm.

Several acini are also in this intermediate part with a lining of one layer of cubical epithelium and containing a small amount of colloid-like substance.

Diagnosis: Large cyst of the hypophysis with pressure atrophy of the anterior lobe. The thyroid gland is unchanged. In sections of the five parathyroid bodies which were found, the only change is a cyst in one of them, 3 by 4 mm. in size; its wall lined by a layer of cuboidal epithelium; there is a small amount of adipose tissue, chiefly in the stroma of these sections; in the cortex of the adrenals the normal amount of lipoid material; the prostate, testes and seminal vesicles normal; epididymides densely infiltrated by lymphocytes, with no indication of either syphilis or tuberculosis.

Remarks: Here, with an almost complete atrophy of the gland, due to the pressure exerted by the large cyst, we have no change which might be ascribed to hypophyseal dystrophy. The eye symptoms and the exaggerated patellar reflexes were evidently due to pressure.

The statement that the patient had been drinking heavily for three weeks may mean that at that time headaches developed and the patient drank because alcohol, among a certain class of working people, is the only remedy used to alleviate pain.

Case 3.—On Nov. 20, 1915, a man, 52 years old, was brought to the Cook County Hospital to the service of Dr. E. W. Andrews in coma with no history except of illness beginning the day before preceded by headache. Respiration was stertorous and Cheynes-Stokes type; the pulse rapid; the pupils were small and did not react to light; both arms and legs were flaccid and there was involuntary micturition. The nose was filled with old dried blood; the cerebrospinal fluid was under increased pressure and turbid; the pulse became rapidly weaker and five and a half hours after entrance he died; clinical diagnosis, cerebral hemorrhage.

It was subsequently learned that six years before he had fallen three stories from a scaffold and sustained a fracture of the left ankle and, it was thought, a basal skull fracture as well. He was unconscious for hours and delirious a week; his vision, especially in the right eye, remained impaired.

Necropsy (Dr. E. R. LeCount): This is the body of a moderately obese white man, 45 years old; weight, 143 pounds;

Fig. 5.—Photograph of a single section 30 by 28 mm. in diameter: A masses of epithelial cells; B, cysts, separated by thin-walled septa (dia. 4).

height, 169.5 cm., with thick, heavy trunk, heavy shoulders, the left leg amputated; muscular development fair; body framework relatively heavy; the hands slender and not muscular. There is no injury of the pericranial tissues. When the calvarium is removed, the dura is very tense and blue. There is nothing but dark-red clotted blood in the superior longitudinal sinus. The spinal fluid is slightly turbid.

In the region of the hypophysis there is a reddish tumor mass, firmly adherent to the sphenoid bone; it is about the size of a walnut and is very soft. The cavity of the nasopharynx is continuous with the sphenoidal sinus on the right side and there is a little of the reddish tumor tissue here. There is no change of the clivis. The skull is unbroken. The brain after hardening has flat cerebral convolutions and the sulci are almost obliterated. The large veins of the leptomeninges are compressed and ribbon-like. The leptomeninges of the tip of the frontal lobes, the cephalad portion of the temporal lobes and inferior third of the parietal lobes over the interpeduncular space are opaque and raised by greenish-yellow material. The arteries of the base of the brain are collapsed and grossly normal. The optic chiasma and surrounding structures are covered by tissue containing thin bony lamellae, closely adherent to and overlapped by dura, the pia arachnoid and a mass of tumor tissue of a very mottled appearance in which the chiasma with part of the optic tract and each optic nerve are embedded. In looking for the hypophysis no special structure can be differentiated in the hollow of the sphenoid bone but similar tumor tissue is found mixed with brown and yellow material. The tumor presses deep into the interpeduncular space and penetrates the third ventricle. Surfaces of coronal segments of the brain are pale; all the ventricles enormously dilated; the lateral ventricles measure 2.5 cm. transversely at the anterior commissure; the septum pellucidum and the fornix are soft; the ventricular ependyma is stained dark brown and coarsely granular. There is no other gross change.

Anatomic diagnosis: Tumor of the hypophysis cerebri; disseminated fibrinopurulent leptomeningitis; edema of the brain; internal hydrocephalus; granular ependymal sclerosis.

Histology: About one half of the sections of the tumor examined consist of round spaces containing blood; in most of these there is no lining that would make them appear to be veins or blood channels but their sharp contour and demarcation rather suggests the latter than hemorrhages. A few on the other hand are obviously the result of hemorrhages. Two kinds of tissue are between these collections of blood; one is the normal hypophyseal tissue, greatly disarranged and increased in amount from hyperplasia, the other is the product of inflammation.

The tumor is surrounded by a thin membrane with disseminated masses of lymphocytes on the inner surface of the latter which penetrate deep into the growth and are dispersed throughout between the strands of epithelium. Some of the smaller vessels are surrounded by masses of similar

cells. There are several foci of necrotic tissue filled with polymorphonuclear leukocytes, lymphocytes, blood, the result of fresh hemorrhage, fibrin and giant cells. The masses of apparently normal epithelial strands make up about one half of the section. Such cells are well defined, irregular in size, with a moderate amount of cytoplasm, staining purplish pink with hematoxylin and eosin; dark purple with phosphotungstic-acid hematoxylin; and pale blue with the Mann's stain; the nuclei are dark, round or oval; some have a ragged appearance and some are crescent shaped. The cells nearer the zone of necrosis are hydropic with invisible or vacuolated protoplasm and large pale-staining nuclei.

Diagnosis: Basophile-cell adenoma of the hypophysis; hemorrhage into the tumor with secondary infection.

Remarks: According to Benda, Erdheim and Lewis, it is only the increase in eosinophile cells which gives rise to acromegaly; this would account for the lack of changes of the bones in this case, notwithstanding the marked hyperplasia of the anterior lobe.

Oct. 13, 1919.

ON THE FUNDAMENTAL PHYSIOLOGIC REACTION IN ANAPHYLACTIC AND PEPTONE SHOCK

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The causes of the remarkable differences in the manifestations of anaphylactic and peptone shock in different animals has been the subject of no little speculation. In the dog, anaphylactic and peptone shock are characterized by a marked immediate fall in arterial blood pressure, a simultaneous fall in venous (external jugular-superior vena cava) pressure, a rise in portal pressure, an increase in the volume of the liver, and, at least in peptone shock, an increased flow of lymph from the thoracic duct. It is evident, therefore, that in the dog the flow of blood through the liver is greatly impeded in these conditions. The exact location of the obstruction has not heretofore been determined.

In reasoning from the above facts it appeared that the only possible location for such an obstruction that

would explain all of the facts was not in the extrahepatic splanchnic area, nor in the portal vein and its intrahepatic branches, nor in the intralobular capillaries, but in the hepatic vein and its branches. It has been shown that a fall in blood pressure such as is seen in the dog is not characteristic of anaphylactic shock of the guinea-pig (Auer and Lewis), nor in the rabbit (Auer), nor in peptone shock in the guinea-pig (Hirschfelder). In searching for a reason for this difference a study has been made of the comparative anatomy of the hepatic vein in different animals. It has been found that the hepatic vein in the dog differs from that of the guinea-pig, rabbit and other herbivorous animals examined, in the relatively enormous amount of smooth muscle which is present in its walls. This study, made in collaboration with Dr. L. B. Arey, will be published later.

It appears very probable, therefore, that the fundamental physiologic reaction in anaphylactic and peptone shock in dogs is a spasm of the smooth muscle in the walls of the hepatic vein and its branches. Experiments which make this evident will be published later.

This interpretation of the physiologic mechanism of anaphylactic and peptone shock has certain practical bearings.. (1) It is known that in the guinea-pig the finer bronchioles are "practically nothing but muscular tubes" (Oppel, cited by Auer and Lewis). The characteristic clinical manifestation of these conditions in this animal is a violent dyspnea in which it can get air into its lungs but is unable to get it out. The dog and certain other animals have hepatic veins supplied with exceptionally large amounts of smooth muscle. The manifestations of anaphylactic and peptone shock in dogs have been described above. It seems possible, therefore, that the basis for these differences in the reaction of different animals in shock of this kind is an anatomical difference in the distribution of smooth muscle in the body. It is possible that an anatomical anomaly in the distribution of smooth muscle may account for certain types of asthma and serum reactions in humans.

(2) This observation may also bring peptone shock into relation to surgical and wound shock. It is only necessary to recall that among the theories advanced by various authors who have studied shock under war conditions, is one which makes the absorption of the soluble products of damaged muscle in wounds responsible for the condition. Furthermore, it is obvious that any prolonged spasm of the hepatic vein and its branches, such as occurs in peptone shock in the dog, will lead to the same condition in the general circulation, or at least in the splanchnic area, of sequestration of blood in the venules and capillaries, as was observed by Jackson and Janeway in the shock produced by them by the mechanical obstruction of the vena cava for limited periods of time.

(3) It is evident, also, that in interpreting the results of experiments on dogs, especially those which have to do with blood pressures, this peculiarity of their hepatic vein must be taken into consideration.

Dec. 8, 1919.

AN INTRACELLULAR PROTOZOAN PARASITE OF THE DUCTS OF THE SALIVARY GLANDS OF THE GUINEA-PIG *

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In the course of an examination of the various salivary glands of the guinea-pig for an entirely different purpose, a peculiar protozoan infection of the ducts was observed, which seemed of sufficient interest to warrant further study. Accordingly, a microscopic examination was made of the salivary glands of forty-eight guinea-pigs. Through the kindness of Dr. H. J. Corper, I was able to secure salivary glands from eighteen tuberculous guinea-pigs that came originally from Pennsylvania and had been brought here but a

* The complete report with illustrations is printed in The Journal of Infectious Diseases, 1920, 26, 347.

few days before they were killed. The kidneys of most of these animals were also examined, as they are sometimes the seat of a coccidial infection. The intestines, unfortunately, were examined in only few cases. The disease apparently causes the animal very little, if any, inconvenience and no gross pathologic changes were distinguished in the glands. On microscopic examination it was found that glands from twenty-six of the forty-eight guinea-pigs were infected. The infection occurred in about the same proportion of cases in the guinea-pigs obtained from Dr. Corper and in those from our own laboratory. The ducts of the serous portions of the glands are the favorite location of the parasite, but they are occasionally found in the ducts of the mucous glands, especially if the infection is severe. Many of the guinea-pigs had very mild infections, and the chief change aside from the presence of parasites in the cells of the ducts was a small amount of mononuclear infiltration about affected ducts, and in presumably early cases even this was lacking. In the cases in which the process was advanced, considerable portions of the gland were involved and more or less destruction of ducts and glandular tissue was evident.

The protozoan, as it most often appears in the cells of the ducts of the salivary gland, is an encysted organism of irregular, round or oval contour. In its most conspicuous and fully developed form it practically replaces the host cell which still retains its relations to the duct wall. The center is occupied by a round or oval body of irregular outline which stains deeply and unevenly. Around this central or restiform body is a rather wide, lightly stained zone, and outside of this a peripheral zone or capsule, which may vary considerably in width, the widest part being that directed toward the lumen of the duct.

From a study of the parasite it appears that the chromatin condenses at various points on the surface of the central body, and smaller bodies bud off and proceed through the intermediate zone to the periphery where they possibly undergo further division. These smaller, deeply stained bodies of irregular outline and unequal size, are seen in various stages of separation

from the central body and in various positions in the intermediate zone, and in some instances the chromatin material forms bands of considerable width extending from the central body to the border of the peripheral zone (Fig. 5). The appearance of radiating lines from the central body to the periphery at a certain stage of development is evidently the result of this budding off process.

Considering the large number of round, lightly stained bodies, which appear in the peripheral zone of the parasite at a certain stage of its development, and the comparatively few more deeply stained, irregularly shaped bodies seen in the process of separation from the central body and in the various stages of progress toward the peripheral zone, it seems not unlikely that further division of the latter bodies takes place when they reach the outer part of the intermediate zone; this, however, cannot be stated with certainty. The peripheral zone, as previously stated, varies considerably in width and stains more deeply than the intermediate zone, and in the latter stages of development it contains large numbers of round bodies which collect for the most part in the portion of the capsule nearest the lumen of the duct. I have not been able to satisfy myself as to the exact number of these bodies, if indeed there is a definite number given off by each parasite. As counted in the stained preparations, they vary in number in the apparently fully developed forms from 30-40 or more. A form of the parasite which differs somewhat from that just described is seen only occasionally (Fig. 4). It is about the size of the large forms just described. In the intermediate zone is a band apparently made up of small, elongated bodies which seem to radiate from the central body. This band nearly or entirely encircles the restiform body, and is separated from it and from the peripheral zone by a clear space. No rounded bodies are seen in the peripheral zone. Just what is the significance of this form is not evident.

The earliest form of the parasite observed is a small, round, deeply stained body embedded in the cytoplasm of the epithelial cell of the duct (Fig. 3). As the para-

site grows it develops an enveloping membrane or capsule, and later a definite intermediate zone appears between the deeply stained restiform body and the capsule. A form frequently seen is one in which the central body is elongated with the chromatin massed at the two poles.

In infections of long standing one may often find the castoff restiform body in the lumen of the duct and occasionally in the tissue just outside the duct. It appears as a pink stained vacuolated body of irregularly round or oval shape. That the parasite penetrates to the tissues about the ducts in the severed infection seems probable. I have observed what I believe to be young forms in the infiltrated regions about the ducts in which the epithelium has largely been destroyed and occasionally young forms appear in the glandular cells in these cases, but no fully developed types have been observed in these locations. In the severe infections one may find four or five of the organisms in a cross section of the duct, or if the section is lengthwise of the duct, the parasites are arranged side by side, and projecting into the lumen present a sawtooth-like appearance.

It seems evident from the foregoing that we are concerned with the vegetative cycle of an intracellular protozoan, the sexual cycle of which does not occur in this location. Since during this stage of development apparently no organs of locomotion are produced and the parasite becomes encysted, it probably belongs to the class protozoa and from its intracellular position most likely among coccidia. This being the case, we may consider the small round bodies in the peripheral zone of the parasite as merozoits.

Whether the parasite gains entrance to the salivary gland by way of the ducts from the oral cavity or by way of the blood stream is not obvious. If infection takes place by way of the ducts, the progress of the parasite up the duct is against the flow of saliva as the epithelial cells of the distal portions of the ducts are never invaded. Whatever the mode of entrance, it is evident that the larger ducts do not offer favorable conditions for the growth of the parasite.

The parasite stains fairly well by the ordinary staining methods, hematoxylin and eosin, methylene blue and eosin, polychrome methylene blue and eosin and Giemsa.

A routine microscopic examination of the other organs of guinea-pigs was not carried out, except in a few cases in which the results were negative, with the exception of the kidneys. The kidneys of forty-four of the forty-eight guinea-pigs were examined for protozoa, and twelve were found positive. The organisms present were usually few in number and apparently correspond with the forms of Klossiella muris described by Smith and Johnson [1] and Louise Pearce,[2] but appear to have no relation to the parasites in the salivary gland.

Jan. 12, 1920.

HEMORRHAGIC MENINGOENCEPHALITIS IN ANTHRAX

S. JOHN HOUSE

From the Pathological Laboratory of Rush Medical College, Chicago

A REPORT OF THREE CASES

SUMMARY AND CONCLUSIONS

A number of cases of anthrax have occurred in Chicago recently, many of them among workers in the "curled hair" industry. In at least three of these cases there were brain complications and in two of the three anthrax was not suspected until after death. It seems reasonable, therefore, to suspect that from time to time similar cases may go unrecognized. In an effort to eliminate such a possibility a careful microscopic and bacteriologic study should be made of every bloody spinal fluid, provided one is certain that the blood is not a contamination; and especially should this be done if there are symptoms of cerebral irritation.

1. Jour. Exper. Med., 1901-5, 6, p. 303.
2. Ibid., 1916, 23, p. 431.

These cases can be easily recognized at necropsy by the soft, red viscid brain, especially if there is a history of an acute illness not resulting from trauma; and it must be remembered that there may be one of at least two types of gross changes—either the brain with the characteristic intracerebral hemorrhages or the brain with blood only in the membranes. On account of the large quantity of blood which is sometimes present it would be easy for one who had not seen such brains to attribute the cause to trauma, but this may be avoided by recognizing the inflammatory quality of the changes and by checking up with stained smears of the exudate.

The lesions in the brain in anthrax are essentially extravascular, meningo-encephalitic, and the acute hemorrhagic nonpurulent nature of the inflammation with destruction of tissue by edema is similar to that produced by anthrax in other places of the body. With suitable stains large numbers of bacilli may be found in these lesions.

The infection of one of the brains of this series was evidently by the hematogenous route, first, because the primary focus was so far removed (intestine), and second, because of the finding of small bacillus-containing foci of edema and dissection along the vasa vasorum of the leptomeningeal vessels.

Jan. 12, 1920.

CONGENITAL BILATERAL HYDRONEPHROSIS

DUPLICATED LEFT URETER, AND A LARGE PERSISTENT LEFT GÄRTNER'S DUCT IN A NEW-BORN

From the St. Luke's Hospital Laboratory, Chicago

EDWIN F. HIRSCH

Duplication of a ureter is one of the commonest urinary tract anomalies. There are examples of this anomaly where the relation of the additional duct to

other pelvic structures has peculiar anatomic or clinical interest. It is commonly known that when both ureters end in the bladder separately their openings lie one behind or above the other, or less frequently side by

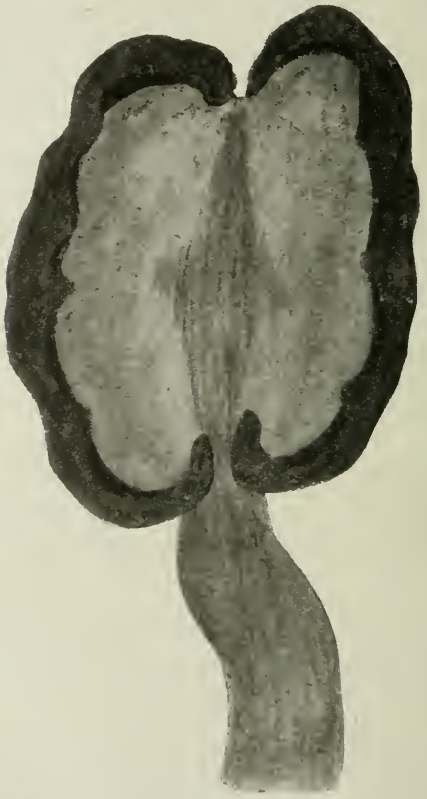

Fig. 1.—Right kidney. Sketch illustrating hydronephrosis and the extent of tissue atrophy.

side, and that the ureter from the upper pole of the kidney ends caudal, medial, or caudal and medial to the terminal end of the other ureter. While aberrant accessory ureters have been reported ending in the

urethra, seminal vesicles, vas deferens, uterus, or vagina, this report concerns only such an anomalous relationship with Gärtner's duct.

A review of the literature fails to disclose any number of such reports, although without question those records of accessory aberrant ureters ending in the uterus, the vagina, and in some part of the vaginal vestibule have to do with persistent portions of Gärtner's duct functioning as a ureter. Tangl [1] reported a duplicated left ureter in a 65-year-old woman, the uterus fusing 3 cm. below the kidney to form a single ureter that ended blindly in the lateral part of the vagina 3 cm. below the external os. From the end of this ureter there extended upward and outward for 6 cm. a persistent Gärtner's duct. The kidney supplied by this ureter was atrophic, 2.5x1.2x0.5 cm. in its greatest dimensions. Hartman [2] in 1913 collected fifteen instances of undoubted aberrant accessory ureters in the female and added one of his own. All of these ended in the vagina, the vaginal vestibule, or adjacent to the urethral meatus. There were others not so clearly reported, making then a total of twenty-five. These do not include Tangl's report, or those observed in fetuses. Sammler's [3] report some time later mentions two others since Hartmann's review, and adds one to make at that time twenty-eight.

This report concerns a female child that lived seventy-two hours and forty minutes after birth. With other anomalies, a postmortem examination demonstrated an aberrant accessory left ureter ending in a large persistent Gärtner's duct. The clinical notations and postmortem observations are given in the following paragraphs:

Clinical Record.—The mother, a white American housewife, 42 years of age, was admitted as a iii gravida in the first stages of labor on Oct. 30, 1919, at 7 a. m., to the service of Dr. Charles Paddock, St. Luke's Hospital, Chicago. Because of a cicatricial stenosis of the cervix an abdominal cesarian

1. Tangl, F.: Beitrage zur Kenntniss der Bildungsfehler der Urogenitalorgane, Virch. Arch., 1889 (118); 414-431.

2. Hartmann, Joh.: Zur Kasuistik und operativen Behandlung überzahliger aberranter Ureteren, Zeitsch. f. Urol., 1913, (7); 429-446.

3. Sammler, A.: Zur kenntniss der aberrierenden überzahligen Ureter, Zeitsch. f. Urol. Chir., 1914, (2); 241-249.

section was made, and a female child weighing 4 pounds and 6 ounces was delivered Nov. 1, 1919, at 7:15 a. m. Excepting for being small and having a bilateral backward flexion of each hand at the wrist, the child appeared well developed. The following comments by the intern are entered in the clinical record, "11/2/19, baby in good condition; 11/3/19, baby in very poor condition, cyanotic, bowels free, urine free, temperature 101 *R;* 11/4/19, baby became very cyanotic, had labored respirations, and did not retain its food, died at 7:55

Fig. 2.—Left kidney. Drawing locating the accessory pelvis and representing the hydronephrosis.

a. m." On 11/4/19, the child weighed 4 pounds and 3 ounces, and urination is charted three times on 11/2/19, four times on 11/3/19, and once on 11/4/19.

Postmortem Examination.—The body is a symmetrical fairly well nourished female child, 45 cm. long. Both wrists are flexed so that the palm of each hand lies flat on the flexor surface of the forearm. These surfaces are directed backward, and the prominence of each elbow is directed laterally away from the body. In the peritoneal cavity there

are 3 to 5 c..c of clear yellow liquid. The skeletal muscles are pale pink, the lower liver margin is 2 cm. below the costal arch. The pericardial sac contains slightly more than the usual amount of clear yellow fluid. The usual amount of thymic tissues is present, and the lymph glands generally are not unusually large. The heart structures appear normal for a newly born child, there being the usual patent ductus Botalli and foramen ovale. The posterior portion of the right lung is somewhat firmer from hypostasis. The adrenal glands are normal.

Urinary system. The right kidney (Fig. 1) is 5 cm. long. Its parenchyma is reduced to a width of 3 mm., the renal pelvis being widely dilated. Immediately below the usual upper anatomic constriction the ureter is twisted somewhat on itself, and dilated to a maximum circumference of 1.4 cm. In its middle portion this dimension is 1 cm. The lower end of the ureter terminates blindly beneath the bladder mucosa at the usual site for an opening (Fig. 3).

The left kidney (Fig. 2) is 4 cm. long. The width of its parenchyma average 8 mm., the pelvis being moderately dilated. It has two ureters, the one from the lower pole draining almost the entire kidney has a circumference of 7 mm. in its middle portion. Its lower end terminates with an opening 0.5 mm. in diamter into the urinary bladder (Fig. 3). The second ureter lies in front and medial. It is a widely dilated sac filled with clear yellow fluid, when opened having a maximum circumference of 2.8 cm. It ends above in a rudimentary pelvis 2 to 3 mm. in diameter near the upper pole of the kidney. In the lowest part of the broad ligament to the left of the cervix it suddenly constricts and ends with two small folds of its lining mucosa (Fig. 3). Continuous with it is a closed duct leading into a nodule of fibrous tissue 1.8 by 1.1 by 0.6 cm. This lies opposite the lower portion of the uterus and the upper portion of the vagina, and contains a very much compressed and flattened duct. On a level with the external cervical os the duct passes at right angles into a papillary elevation 1.1 cm. long, 0.5 cm. wide, and 0.6 cm. high in the left vaginal wall opposite the external cervical os. Along the upper left lateral wall of the vagina to the hymen is a ridge of tissue 2.7 by 0.4 by 0.4 cm. in which this duct continues, and ends blindly in the hymen. There are several small pits on the external surface near this termination, but none connect with the duct. The duct is lined by columnar epithelium. There is also a ridge of tissue 2.7 by 0.7 by 0.6 cm. in the anterior midline of the vagina, but it contains no duct.

The uterus, the right and left fallopian tubes, and the right ovary are normal, the left ovary contains a thin-walled cyst 0.7 cm. in diameter filled with clear fluid. There is no abnormality of the urethra. The anus is patent and normal in

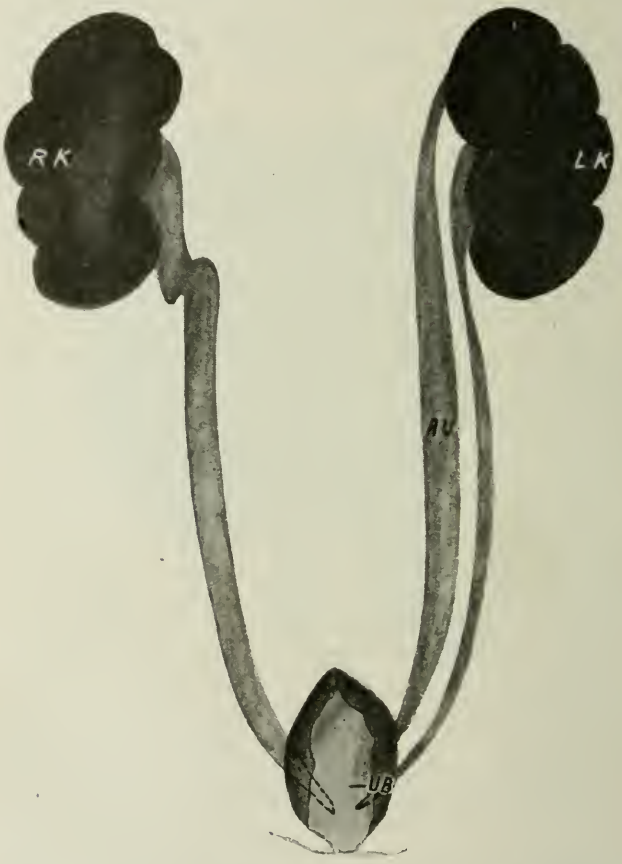

Fig. 3.—R. K., right kidney; L. K., left kidney; A. U., accessory ureter; U. B., urinary bladder.

position. Thirty-five cm. from the cecum is a Meckle's diverticulum of the small bowel 1.2 by 0.6 cm. The brain is soft and very moist.

Discussion: The interpretation of this congenital anomaly is made clearest by considering the embryologic origin [4] of the ureter and the primitive structures with which it is related. This concerns especially the wolffian duct which in early embryonal development opens into the primitive cloaca (Fig. 4). Where it arches forward after approaching the dorsal wall, a small diverticulum develops ultimately to become the

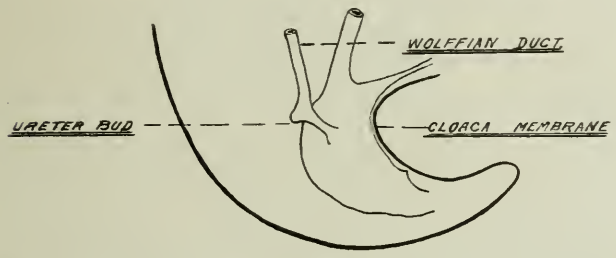

Fig. 4.—Diagrammatically illustrating the origin of the ureter in the Wolffian duct, and the relation of these structures to the cloaca.

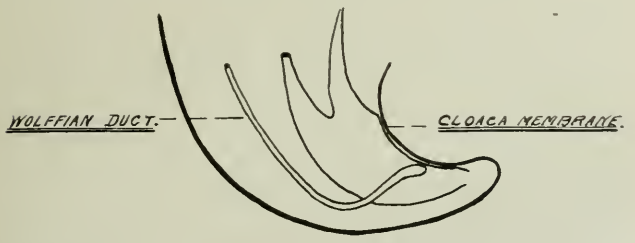

Fig. 5.—Representing the relation of the Wolffian duct to other caudal structures.

ureter and renal pelvis. The presence of two ureters is explained by the anomalous development [5] of two such diverticula on the wolffian duct, one above the other, the lower one being the usually formed ureter bud, the upper one the accessory. While in the male the wolffian duct becomes the vas deferens and certain

4. Kiebel and Mall: Handbuch der Entwickelungsgeschichte des Menschen, Leipzig, Volume 2, 1911.

5. Meyer, Robert: Zur Anatomie und Entwicklungsgeschichte der Ureterverdoppelung. Virch. Arch., 1907, (187) 408-434.

related structures, in the female only vestigial remnants persist as Gärtner's duct. This may pass from the epoöphoron through the broad ligament at first parallel with the fallopian tube, then more diagonally as the base of a triangle whose opposite angle is formed by the uterine portion of the fallopian tube and the body of the uterus. Near the level of the internal uterine os the duct passes into the uterine substance, gradually approaching but not reaching the mucosa. From the upper portion of the cervix it enters the lateral vaginal wall and passes caudally along the middle of the lateral vaginal wall. In the lowest part of the vagina the duct approaches the dorso-lateral wall and ventrally reaches the lateral part of the hymen. The external opening usually is close to the margin of the hymen, rarely more lateral in the nympho-hymen sulcus of the vestibule. (See Fig. 5.) In extremely rare instances Gärtner's duct persists complete. It is lined by columnar epithelium.

This brief summary of the wolffian duct embryology enables an explanation of the relation of the accessory ureter to the duct described. The structure with which the lower end of the accessory ureter is continuous is an unusually large remnant of a wolffian duct. Meyer [5] accounts for the caudal, medial, or caudal and medial position of the accessory ureter to the usual by a craniocaudal 180 degree rotation of the terminal portion of the wolffian duct above that portion. If the upper or accessory ureter arises in the wolffian duct above that portion which ultimately is taken into the wall of the urinary bladder, its termination will be in a derivative of the wolffian duct. Wimmer [6] thinks that growth differences rather than rotation are sufficient to account for the ultimate termination of the accessory ureter.

Congenital deformities commonly are multiple. In addition to the accessory aberrant left ureter and the persistent Gärtner's duct described, there were in the body of this child also an incomplete external rotation of the upper extremities, a right complete and a left

6. Wimmer, Hermann: Doppelbildungen an den Nieren und ein Versuch ihrer entwicklungsgeschichtlichen Deutung, Virch. Arch., 1910, (200) 487-522.

incomplete atresia of the ureters by folds of the bladder mucosa, and a Meckle's diverticulum of the small bowel. The extensive injury to kidney tissue probably caused death.

SUMMARY

In a female child dying seventy-two hours and forty minutes after birth, the following congenital deformities were noted:

1. An accessory aberrent left ureter ending blindly in a large persistent Gärtner's duct.
2. Right complete and left incomplete atresia of the ureters by folds of the bladder mucosa.
3. Incomplete external rotation of the upper extremities.
4. Meckle's diverticulum of the small bowel.

March 8, 1920.

A SIMPLIFIED PLATE METHOD OF PARTIAL OXYGEN TENSION IN THE CULTIVATION OF THE GONOCOCCUS

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From the John McCormick Institute for Infectious Diseases.

The idea of growing the gonococcus and other organisms under reduced tension is not new. Wherry and Oliver [1] have demonstrated the value of the method. Chapin [2] and more recently Maitra [3] have used it with success in obtaining primary cultures on a variety of mediums.

The advantage of using plates in the isolation of the gonococcus is obvious when it concerns the isolation of gonococci mixed with other bacteria. Here, streaking of the material over a large surface is necessary to obtain discrete colonies. The simple method of using partial oxygen tension plates here described has been devised and employed with success in this laboratory.

1. Wherry, W. B., and Oliver, W. W.: J. Infect. Dis. **19**: 23 (Sept.) 1916.
2. Chapin, C. W.: J. Infect. Dis. **23**: 342 (Oct.) 1918.
3. Maitra, G. C.: Indian J. M. Res. **7**: 219 (July) 1919.

Two inoculated plates, one with the gonorrheal material, and the other with *B. subtilis*, are placed together with the open sides facing each other. Then a closed rubber band 2½ inches wide by 3½ inches in diameter encircles both, enclosing the edges but allowing aerial communication between them, as shown at the right. Satisfactory bands may be obtained by cutting wide rubber tubing into pieces of the required width. The simplicity of this method makes it practical for the small laboratory and, in addition, permits of individual cultures being examined without disturbing others, as is necessary with several cultures in a single jar. The rubber also serves equally well for air exclusion plates, which have a distinct advantage over open aerobic plates in gonococcus cultivation; but they are inferior to the partial oxygen tension method just described, especially in obtaining primary growth. Parallel plates have been tested with a variety of mediums, and the best growth was obtained on nutrient bactoveal agar in which dibasic sodium phosphates were substituted for sodium chlorid.[4] Ascites fluid and defibrinated goat blood were added in the approximate proportion of 2 c.c. of ascites fluid and 0.5 c.c. of blood to each Petri dish before pouring the plates. A fair growth has resulted with this medium minus ascites fluid.

Cultures of gonococci have been obtained in several cases of chronic infections in which the gonococcus could not be identified in smears. In all the acute cases of gonorrheal urethritis there was a profuse growth, parallel aerobic plates showing fewer and smaller colonies.

Recently this scheme has been used in place of the culture of *B. subtilis* with good results: A quantity of sodium bicarbonate is placed in the Petri dish instead of the culture of *B. subtilis*, and at the same time a small glass tube containing 0.5 c.c. of 1 per cent. sulphuric acid is introduced so that when the plates are enclosed in the rubber band the two chemicals come into contact with each other. In this way sufficient carbon dioxid is liberated to produce a favorable tension.

March 8, 1920.

4. Martin, W. B.: J. Path. & Bacteriol. **15**: 76, 1911.

ON THE RELATION OF THE CEREBRAL HEMISPHERES TO ARTERIAL BLOOD PRESSURE AND BODY TEMPERATURE REGULATION *

PRELIMINARY NOTE

F. T. ROGERS

Hull Laboratory of Physiology, University of Chicago

It has been pointed out elsewhere [1] that removal of the cerebral hemispheres and the optic thalamus destroys the mechanism for regulating body temperature and reduces the animal to a cold-blooded condition. This loss of ability to maintain a normal body temperature after extensive traumatic injury around the third ventricle is common to all warm-blooded animals from man to birds. Only one group of warm-blooded animals so far as the literature indicates will long survive such an operation. Dogs, cats and monkeys may be kept alive for several days, but in the dog, on which most work has been done, one week is the maximum recorded length of life. In birds, which are warm-blooded animals, with proper precautions the animal may be kept alive for several months.

In an attempt to get at the factors that lead to this loss of ability to regulate body temperature studies on the circulation of the blood in these animals have been started. A method was devised for measuring arterial pressure in the pigeon and determinations have been made before and after reduction of the animal to the cold-blooded condition.

In the normal adult pigeon under all stages of ether anesthesia the blood pressure in twenty-three birds ranged between the extreme limits of 98 to 180 mm.

* Read at joint meeting with Chicago Neurological Society.

1. Amer. Jour. Physiol., 1919, Vol. 49, p. 271.

mercury. The average value of these determinations was 121 mm. (Table 1).

TABLE 1.—ARTERIAL PRESSURE—NORMAL BIRDS

All Readings in Mm. Mercury					
126	116	114	118	108	122
106	160	100	102	122	98
142	110	124	119	136	110
138	150	124	110	124	
Average, 121					

Measurements of arterial pressure have been made on six pigeons reduced to the poikilothermous condition by removal of the thalamus and hemispheres. These have been made at time intervals of from three to thirty days after operation so as to exclude the possibility of dealing with the acute effects only. The body temperature of these birds was set at various levels by changing the temperature of the incubator in which they were kept. The results of this experiment are given in Table 2.

TABLE 2.—ARTERIAL PRESSURE—POIKILOTHERMOUS BIRDS

Days to Recover From Operation	Body Temperature	Blood Pressure
3	29 C.	78 Mm.
5	28 C.	84 Mm.
13	28 C.	95 Mm.
5	36 C.	104 Mm.
15	29 C.	93 Mm.
29	41 C.	85 Mm.
3	31 C.	80 Mm.

These results at once suggested that the loss of temperature regulation was the result of lowered arterial pressure. However, as a control on this conclusion, blood pressure readings were made on birds from which the hemispheres only had been removed, thalamus being left intact, and with therefore normal body temperature. It was found, somewhat as a surprise, that loss of the hemispheres also led to a similar fall in arterial pressure, though not quite so extensive (Table 3). In different cases this ranges from 10 to 20 per cent. It has long been known that in acute experiments removal of the hemispheres leads to a slight

fall in arterial pressure, but as is evident from the time figures given, this fall is more than a mere temporary shock effect and may persist as long as two and one-half months after decerebration; and this in animals in which we have been accustomed to think the shock effects are at a minimum.

TABLE 3.—ARTERIAL PRESSURE—DECEREBRATE BIRDS
Body Temperature Normal

Normal Pressure Before Operation	Days to Recover From Operation	Blood Pressure After Operation
128 Mm.	8	105 Mm.
156 Mm.	11	97 Mm.
108 Mm.	3	93 Mm.
98 Mm.	16	96 Mm.
134 Mm.	3	98 Mm.
142 Mm.	5	122 Mm.
124 Mm.	5	103 Mm.
.....	75	105 Mm.
.....	21	96 Mm.
.....	6	87 Mm.
.....	11	91 Mm.

A comparison of the arterial pressure in the two sets of operated birds, both with hemispheres removed, but the one with ability to regulate body temperature and the other with temperature regulation impaired, indicates a greater degree of depression in the latter series. However, the difference is so slight that it suggests that the lowering of body temperature must be due to some other factor than that of circulatory disturbance alone. I suspect that the disturbance in body temperature is due not only to the vascular disturbance but also to lessened heat production, in part if not wholly due to injury of the subcortical motor centers for the skeletal muscles.

In concluding it may be added that the above described effects are very inconstant in localized lesions of either the hemispheres or thalamus. Hence the effects described are, in this report, confined to those following total extirpation. Certain effects of lesser lesions will be described in the full report to be given later.

SUMMARY

Removal of the cerebral hemispheres in the pigeon, leaving the thalamus intact and body temperature normal, leads to a constant fall in arterial pressure of from

10 to 20 per cent. This fall comes on immediately and persists for as long as seventy-five days after the operation.

Removal of the hemispheres and thalamus leads to a loss of temperature regulation and usually to a slightly greater fall in arterial pressure than does loss of the hemispheres alone.

It is possible by a combination of external warmth and intracranial pressure increase to bring the blood pressure nearly to the normal value without restoring the temperature regulating mechanism.

DISCUSSION

Dr. S. A. Matthews said that Isenschmid and Kiehl[2] have published experimental results indicating that the caudate nuclei and the anterior part of the optic thalami may be removed from rabbits with only a temporary change in the heat regulatory mechanism. When, however, the posterior and ventral portions of optic thalami were removed the animals became poikilothermal. Also Citron and Leschke[3] claim that destruction of the median portion of the between brain on the boundary of the corpus quadrigeminum and the optic thalami anterius make rabbits poikilothermal. In dogs it is quite easy to gain access into the third ventricle by drilling a hole about 5 mm. in diameter through the sphenoid bone just back of the optic chiasm. Of course, this will encroach somewhat upon the pituitary body, but through such an opening lesions can be made in the basal ganglia. In one dog in which he made a lesion in the anterior part of the optic thalami and which involved the principle, accessory, and dorsal nuclei of the tuber cinereum, and after which the animal lived for three weeks, the temperature gradually fell and during the last two days of life was as low as 22 C. The animal gradually developed a lethargic condition. When the animal was placed in an incubator at 31 to 32 C. the temperature would go up to normal, and the reflexes would approach a normal state. Evidently from Dr. Rogers' results on birds and the results of others on mammals, the thalami contain the seat of the heat regulation. Just how they bring this about, whether by increased heat dissipation or by diminished oxidation has yet to be shown.

2. Isenschmid and Kiehl: Arch. f. Exp. Path. u. Pharm., 1912, Vol. 70, p. 109.

3. Citron and Leschke: Zeit. für Exp. Path. und Ther., 1913, Vol 26, p. 161.

Dr. I. Leon Meyers asked whether any examination of the temperature or arterial pressure had been made in dogs after producing in them the state of decerebrate rigidity.

Dr. Lewis J. Pollock asked what was done in these operations relative to closing the cranium so as to keep intact the intracranial pressure, inasmuch as this would probably have considerable to do with the general blood pressure.

Dr. F. T. Rogers (closing) said that the three questions are all very significant. In reference to Dr. Meyer's question, this point has been tested out in the dog and it is known that the loss of the cerebral hemispheres leads to a depression of the blood pressure. In the dog there are certain complications, however, due to anesthesia and to changes in the muscle activities involved in decerebrate rigidity. Dr. Matthews had struck the keynote of the problem in referring to calorimetric controls in this work. It is evident that in the temperature regulation one must consider both heat production and heat loss. The heat loss in the bird seems to be principally through the skin and secondarily through the lungs by expiration. As to heat production, he was inclined to think, on the basis of evidence, not yet conclusive, that there is deficient heat production resulting from diminished muscle activity. As to Dr. Pollock's remark, his is the same question that has been raised by others in the last few years. In an article recently published by L. M. Moore it is stated that a rise in body temperature does not follow puncture of the corpus striatum unless it is associated with increased intracranial pressure. In this report, cases are not included where there is clear evidence of increased intracranial pressure. Furthermore, it may be added that it is an open question of how much of the effects of hypophysectomy or irritation in the hypophyseal regions are due to secondary disturbances of the adjacent brain stem.

April 12, 1920.

Joint meeting with the Chicago Neurological Society

THE MORPHOLOGY OF THE SYNAPSE IN VERTEBRATES*

GEORGE W. BARTELMEZ
Department of Anatomy, University of Chicago

In no field of investigation has the personal factor played a more prominent part than in the structure of the central nervous system, especially in the matter of the synapse. The chief reasons for this are the complexity of the tissue, the minute proportions of the structures involved with the attendant difficulties of interpreting the microscopic picture and also the prominence which technical procedures must play in the study. Since the Neurone Theory accepted the Cajal doctrine of the synapse by contact, it has been most successfully attacked from this aspect. If one be inclined to question whether the Golgi and Cajal methods give complete pictures of the strictly nervous elements of the tissue, then the bulk of evidence at the present time favors protoplasmic continuity at the synapse. This is significant since the findings favoring continuity are positive as contrasted with the negative findings for contact. On the other hand, our present knowledge of the structure of protoplasm and of the effects of current histological methods on it are beginning to imbue us with a hopeful scepticism concerning the reliability of most cytological preparations, particularly of the central nervous system. We need more perfect methods and there can be little doubt that, when developed, they will discredit much generally accepted work.

No other tissue approaches the central nervous in complexity, so it is worth while to enumerate the number of histological elements which enter into the composition of the gray matter. Five groups of structures are recognized:

* Read at joint meeting with Chicago Neurological Society.

a. The undoubtedly nervous elements; the perikarya, their dendrites, axones with collaterals and the ramifications of afferent axones.

b. The neuroglial elements; the protoplasmic glia syncytium, which is probably the Golgi net of Bethe, the neuroglia fibers, and in most preparations the products of their disintegration.

c. Myelin sheaths or the products of their partial solution, such as neurokeratin nets.

d. The fluid substratum or ground substance which certainly contains coagulable proteins.

e. Blood vessels with their accompanying collagenic tissue.

All of these must be taken into account, and besides there are the distortions following the solution of various elements and the shrinkage due to dehydration and embedding which add to the difficulty of interpreting the microscopic picture. It is essential that very thin sections be used if reliable observations are to be made, and even then it is very difficult to understand oblique sections.

Nowhere has the personal factor so insidiously entered into the problem as through the technical procedures. Since no one has thus far been able to study an uninjured nerve cell nor the effects of various fixing fluids on it, the criteria of a well preserved preparation have remained largely subjective. With the development of special methods for the various constituents of nervous tissue the tendency has grown to place implicit faith on the microscopic preparation. The study of many methods has convinced me that in most types of synapses the appearance of contact or continuity can be produced by using appropriate fixatives, or by sufficiently hydrating the coagulated protoplasm with long washing treatment with alkaline solution, etc. Thus there can be no doubt that the descriptions of so careful an observer as Hans Held are perfectly objective, but I believe that his methods have produced fundamental changes in the relations of the nervous elements in the synapse. All who have worked largely with material fixed in formol, and especially with the Bielschowsky technic, have supported

the continuity theory, a fact which is to be associated with the swelling effect of the formol solution on nerve fibers, even when it has been "neutralized" with magnesium carbonate. The only material in which nothing is stained but indubitable nervous structures is a successful Cajal preparation. Of course, in the case of most synapses there is no answer to the criticism that the method does not stain *all* the nervous elements; but in at least one case there is an answer, as will appear shortly. Most other preparations show additional elements, thus complicating the picture and these are preferred by the advocates of continuity. Metallic impregnation methods come nearest to giving a specific stain for nervous elements, but even here the specificity is only relative. Slight changes in the method may give very different pictures, and when the glial elements are at all visible it is usually impossible to distinguish them from nervous elements by color alone; no matter how good the preparation, it is never possible so to differentiate them throughout an entire cross section of the brain. In any case it is essential that the silver methods be checked by other methods which have been shown to produce minimal change in form relations when used on tissues which can be studied fresh. Unfortunately, the ubiquitous lipoids of the nervous system reduce many of the reliable fixing agents so rapidly that it is impossible to obtain adequate fixation even in small pieces of tissue. Unless the lipoids are at least partly preserved, the distortions due to their solution are so great as to invalidate any conclusions concerning the minute structure of most synapses.

Up to the present time, only one synapse has been found in which the elements are large enough to give unambiguous microscopic pictures in all types of preparations. In 1915,[1] I called attention to certain large bulbous endings of the vestibular nerve on the lateral dendrite of Mauthner's cell in the catfish, *Ameiurus melas*. Here giant vestibular fibers terminate in club endings, the largest of which are 7μ, the average being

1. Mauthner's cell and the nucleus motorius tegmenti, Jour. Comp. Neur., Vol. 25, p. 87, 1915.

4.6μ in diameter as measured in sections. The endings lie in contact with a sword-shaped dendrite of a large cell, the axon of which extends throughout the spinal cord and makes direct connections with all the motor centers concerned in swimming. It readily shows the effects of adverse conditions as do other highly specialized cells in the nervous system. Marui[2] has studied Mauthner's cell and some of its synapses under both normal and experimental conditions, but unfortunately he did not find these endings on the lateral dendrite which would have given him really clear evidence. This failure is probably due largely to a lack of familiarity with the teleost brain. Since he came to the conclusion that fibers from the dense pericellular feltwork enter into the body of Mauthner's cell I have gone over the field again, and come to the conclusions stated above; namely, that the technic plays a decisive rôle in the study of such synapses as Marui worked with. In thick sections (8 to 10μ) of formol fixed material, especially in Bielschowsky and Levaditi preparations, one can find pictures which may be interpreted as evidence for the continuity theory of the synapse, *but only in the very delicate synapses about the cell body*. On the other hand, in every preparation I have studied, and this includes formol material, the histological picture of the club endings on the lateral dendrite can be interpreted in only one way: viz., the vestibular endings in every case lie close to the lateral dendrite but *never show any indication of fusion with it*. This leads me to view with the utmost scepticism the reality of the conditions which have been observed by Held, Bielschowsky, Bethe, Marui and others[3] in histological preparations, where there was continuity between different neurons. That is to say, I believe that Held's pericellular nervous terminal net, the fusion of the protoplasm of "endfeet" with that of perikarya, the entrance of pericellular fibrils into the substance of nerve cells and similar conditions are due to post-vital

2. On the finer structure of the synapse of the Mauthner cell, etc., Jour. Comp. Neur., Vol. 30, 1918. The effect of overactivity on the morphological structure of the synapse, ibid., Vol. 30, p. 253, 1919.

3. A complete bibliography of this subject is given in Heidenhain "Plasma und Zelle," Volume 8 of Bardeleben's Handbuch der Anatomie des Menschen, 1911.

fixation or maceration artefacto. Experiments are in progress to test these conclusions in greater detail.

Marui (1919) has recently published the first study on the synapse under experimental conditions. In the much more complex synapses of Mauthner's cell which he studied, no changes in the purely nervous structures were found. His findings in the activities of the glia cells under experimental conditions in exhausted animals are of prime importance, but it remains to be seen whether these were due merely to the very harsh method of "fatiguing" or are due to serious injury of nutritional origin.

DISCUSSION

Dr. C. Judson Herrick said that he naturally had been much interested in watching the progress of the investigation, and in seeing the preparations on which the conclusions were based. Dr. Bartelmez was very frank in expressing himself as a neuronist, with the preconceptions which this implies. He thought the majority of neurologists had been, or still are, neuronists. The facts in the case were very clear in this particular instance. The histologic picture was as unambiguous as the histologic pictures one was in the habit of getting in studies on other tissues. One thing must not be forgotten: Suppose we have a membrane which bounds the protoplasm of the end of the axone as it comes in from the vestibular nerve, and a second membrane which bounds the cell body to which this ending is applied, the nature of these membranes must not be neglected; they are not inert substances, but living tissues. It was still an open question whether to speak of protoplasmic continuity or not. The preparations appeared to show that there were two kinds of living substance intervening between the protoplasm of the first neuron and that of the second. That there was something there which was of tremendous physiologic importance, every one believed, and if we have a contrast between the protoplasm of the first neuron and that of the second and a further contrast between the two protoplasms that constituted the two membranes, there was some ground for the doctrine of discontinuity. Nevertheless, they were all living substances and so it was largely a question of definition whether to speak of protoplasmic continuity or not.

April 12, 1920.

STUDIES ON THE SYMPATHETIC NERVOUS SYSTEM*

S. WALTER RANSON

(ABSTRACT)

It is probable that the sympathetic nervous system is constructed along somewhat simpler lines than those indicated by the description found in most textbooks of histology. It is well established that visceral efferent fibers run through the ventral roots and white rami to the sympathetic trunk, within whose ganglia the majority of the fibers end. Some are continued through the splanchnic nerves to the ganglia of the celiac plexus. These fibers end in synaptic relation with neurons of a second order, often designated as sympathetic neurons, whose axons run to end on involuntary muscle or glandular tissue. Thus two visceral efferent neurons are concerned in transmitting an impulse from the cerebrospinal nervous system to smooth muscle or gland, and these are often designated as preganglionic and postganglionic, with reference to the ganglion which contains the synapse between them.

There are probably no afferent neurons in the ganglia of the sympathetic trunk nor in the collateral ganglia, and no afferent fibers running from these ganglia to end in the spinal ganglia. Dogiel's work, published in 1896, in which he distinguishes both sensory and motor neurons, has not been supported by more recent investigations. Langley has shown, and we have been able to confirm his observations on this point, that after section of a spinal nerve distal to the spinal ganglia all or nearly all of the fibers in the corresponding white ramus degenerate, which would not be the case if any considerable number of afferent fibers of sympathetic origin were directed through the rami into the spinal ganglia. The afferent fibers of the sympathetic trunk and splanchnic nerves are probably all derived from cells in the spinal ganglia.

* Read at joint meeting with Chicago Neurological Society.

Sections of the superior cervical ganglia of man, stained by the pyridin silver technic, display a wealth of dendritic branches arising from the multipolar ganglion cells. These are of two kinds: namely, subcapsular dendrites and extracapsular dendrites. The latter pierce the membranous sheath or capsule, which surrounds the cell, and run long distances in the ganglia, branching repeatedly. The subcapsular dendrites branch and intertwine beneath the capsule, causing it to bulge locally and forming what may be called a glomerulus. When the localized subcapsular mass of dendritic ramifications is formed from the dendrites of one cell it may be called a simple glomerulus. If formed by dendrites from two or more cells it may be designated as a bicellular, tricellular or multicellular glomerulus.

The extracapsular dendrites interlace with untold numbers of fine branching axons, forming an intercellular plexus which occupies the interspaces among the ganglion cells. We are interested chiefly in the axonic ramifications which help to constitute this plexus. Huber and Dogiel claimed that the majority of these fibers were the axons of sympathetic cells in the same or nearby ganglia. And their observations on the composition of this plexus constitutes the only histological evidence worth mentioning for the existence of association neurons in the sympathetic system. Such neurons if present would serve to unite one ganglion with another or the several parts of one ganglion with each other. The physiological evidence, so well presented by Langley, is all against the existence of such association neurons. The important question then is: What is the source of the fine axons in this plexus?

In a number of dogs we cut the cervical sympathetic trunk, thus severing all of the preganglionic fibers which run to the superior cervical ganglion. After time was allowed for degeneration, pyridin silver preparations were made of the superior cervical ganglion. These showed a complete absence of the fine branching axons of the intercellular plexus. These experiments furnish strong evidence that no synapses are

present in this ganglion except those between preganglionic and postganglionic neurons.

The sympathetic trunk of the cat consists of more or less segmentally arranged ganglia bound together by fibers from the white rami. Preganglionic fibers from the upper nine white rami run upward in the trunk to the stellate and superior cervical ganglion. Similar fibers from the white rami below the fourth run downward in the trunk and many of these run through the splanchnic nerves to the celiac plexus. Others terminate in the ganglia of the thoracic, lumbar and sacral portions of the trunk.

The visceral afferent fibers of the sympathetic trunk and splanchnic nerves take origin from the cells of the spinal ganglia. They include large, small and medium-sized myelinated fibers and many which are unmyelinated. These were studied in white rami from which all the preganglionic fibers had disappeared as a result of section of the corresponding spinal nerves proximal to the spinal ganglia. Such partially degenerated rami containing only sensory fibers could be followed into the trunk by a study of serial sections. In the trunk each such ramus forms a longitudinal fascicle which maintains its identity for long distances, and the fascicles from the lower thoracic white rami can be traced into the splanchnic nerves.

The splanchnic nerves of the cat usually contain no appreciable number of postganglionic (i. e., sympathetic) fibers. These nerves are composed of preganglionic visceral efferent fibers from the spinal cord and visceral afferent fibers from the spinal ganglia, both of which reach the sympathetic trunk by way of the white rami and merely run through that trunk to enter the splanchnic nerves. In two out of ten greater splanchnic nerves examined there were also small bundles of postganglionic fibers. In one of these instances it was obvious that these fibers arose from an extra ganglion located on the sympathetic trunk between the first and second lumbar sympathetic ganglia.

These observations have been reported in greater detail in Vol. 29 of the *Journal of Comparative Neurology.*

DISCUSSION

Dr. C. Judson Herrick asked if Dr. Ranson had extended his observations to the peripheral ganglia, and if he could give any suggestions as to whether they would apply equally to the ganglionic complexes of the abdominal viscera, etc.

Dr. Ranson (closing) thought Dr. Herrick's question was very pertinent. He was sorry to say that he had not been able to get a satisfactory preparation of the peripheral ganglia. The technical difficulties involved in the study of the peripheral ganglia are much greater than those encountered in the study of other parts of the sympathetic system. He had tried to be careful to limit his remarks to the sympathetic chain, splanchnic nerves, and the prevertebral ganglia. In regard to these, the physiologic and histologic evidence is in full accord; but in the case of the peripheral ganglia, the physiologic evidence seems to point to something, which we do not have in the ganglionic chain, a mechanism for visceral reflexes that is independent of the cerebrospinal axis.

April 12, 1920.

THE PATHOLOGICAL HISTORY OF THE LUNG STRUCTURE IN BRONCHIAL ASTHMA*

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Most of the theories formulated to explain the etiology of bronchial asthma are based on the conception that the disorder is produced by a spasm of the smooth muscle system of the bronchial tree. This view is given strong support by the apparent relation of certain forms of asthma to anaphylaxis. In the infectious type of asthma there is still a question as to how the bacterial invasion of the mucosa and submucosa produces bronchial stenosis. This mechanism may vary in different types of cases: in some the abundant exudate is undoubtedly an important factor in causing obstruction, in others the infection may lead to profound injuries of the protecting layers of the

* For a complete analysis of this subject see our article in a forthcoming number of the Archives of Internal Medicine.

mucosa, causing minor losses of substance and facilitating the absorption of toxic material.

In the asthma which is caused by foods the specific protein probably gains entrance to the blood or lymph stream through the intestinal mucosa and is carried to the bronchi, where it causes the disturbance.

In asthmas due to inhalation of plant or animal proteins, the specific protein gains entrance either directly through the bronchial mucosa, or is absorbed and carried by lymphatics or blood vessels until it eventually reaches the bronchial musculature.

It is also very probable that various poisons of the type of histamin may be carried by blood or lymph from the intestinal tract or distant foci of infection to the bronchial musculature, causing it to contract.

The anatomical study of the different clinical types of asthma presented here seems to give a rational basis for this varying pathogenesis. Literature contains, as far as we can find, only thirteen case reports on the pathological histology of bronchial asthma, and of these only about 50 per cent. seem on critical examination to be cases of true bronchial asthma. Ellis and Marchand have given the most detailed description of microscopical pathological changes in the bronchial structure, while the others have centered their attention too much on the examination of the character of the exudate, overemphasizing the questionable importance and relationship of Curshman's spirals, Charcot-Leyden crystals and eosinophils to the underlying fundamental mechanism of the condition.

We are very fortunate to add to this group four new cases. (For assistance in obtaining normal and pathological material, we wish to thank Drs. H. G. Wells, Raulston, Boughton, White and Stangl.) Examination of the lungs was made as follows: The intact lungs were fixed in either formalin or Zenker's fluid, were then sectioned, following as far as possible the main branching of the bronchial tree in such a manner that alternate cross and longitudinal blocks of tissue were taken from the hilus to the pleural surface. The sections were stained with hematoxylin and eosin, Mallory's connective tissue stain and Van Gieson's stain.

The *first case*, Mrs. B., an infectious type, is that of a woman, 55 years of age, who had had asthma for two years following a severe bronchitis, and who became despondent during a severe attack, and committed suicide by drowning. The body was in the water about three hours and was examined five hours after death.

Mrs. B., cross and longitudinal microscopic examination of sections. The larger bronchi are empty or contain only a few stringy shreds of mucus in which there are numerous desquamated epithelial cells, numerous mononuclear and polynuclear eosinophil cells, a few polynuclear neutrophil cells and a few small round cells. No crystals or definite Curshman spirals were seen, although the mucus showed evidence of layer formation. The epithelium is for the most part intact, thrown into shallow folds and contains a few goblet cells. The basement membrane is thick and appears hyaline. The layer between the basement membrane and the muscle layer, the subepithelial layer, varies in thickness and structure, in places being thin and containing only a few cells and strands of elastic tissue; in others being thick and containing many small round cells which may be collected about a gland duct or scattered, numerous mononuclear and polynuclear neutrophil cells, a few polynuclear neutrophil cells, a few plasma cells, a few small capillaries and varying amounts of elastic tissue. The muscle layer is well developed and made up of distinct bundles which vary considerably in size and which are separated by thin layers of connective tissue containing a few round cells and eosinophil cells. The mucous glands are very large, the acini being distended by thick mucus and separated more or less from each other by connective tissue in which there are a few mononuclear and polynuclear eosinophil cells, a few plasma cells and numerous small round cells which in many glands completely obliterate portions of the gland tissue. The ducts leading from the glands are distended by mucus and their walls are infiltrated by numerous round cells. In some ducts a definite ampulla is formed between the gland and the muscular layer. The cartilages have a normal structure and arrangement, a few showing calcification.

The structure of the smaller bronchi is similar to that of the larger except that in many the lumen is completely obliterated by mucus. The muscle bundles and mucous glands are well developed throughout and in all cases the cartilages persist longer than the glands in the finer divisions of the bronchi. Many of the bronchiols are completely obliterated by mucus which contains large numbers of eosinophil cells. The walls contain only a small amount of muscle tissue.

The alveoli show only a patchy moderate emphysema and some are filled by a fine granular precipitate. In some portions there are small interstitial hemorrhages.

The second case, Mr. G., also one of the infectious type of asthma, is that of a man, 55 years of age, who had had asthma for six years following a severe bronchitis and who died in the Presbyterian Hospital during an attack. The bronchi and their divisions contained only a small amount of mucus and many fragments of desquamated epithelium. The epithelium is mostly desquamated. The basement membrane is not prominent. The subepithelial layer has a patchy round cell infiltration, very few eosinophil cells, and contains many engorged capillaries. The muscle layer is markedly developed even to the bronchiols. The mucous glands are not large, contain a few foci of round cells and in some places include considerable fatty tissue. The cartilages are normal in arrangement and structure. The bronchial arteries are thick walled. The alveoli show only a moderate emphysemia, some containing a fine granular precipitate.

The third case, Miss L., probably a food asthma, is that of a girl, 17 years of age, who had had asthma since early childhood and who died in the Cook County Hospital of an acute hemolytic streptococcus pericarditis and peritonitis. The larger bronchi are almost free from mucus and desquamated epithelium and the smaller bronchi and the bronchiols are partially or entirely occluded by folded epithelium and mucus which contains fragments of desquamated epithelium and many polymorphonuclear cells. The epithelium which is thick, is partly desquamated and in the smaller bronchi and bronchioles is thrown into folds, which in some of the bronchioles completely occlude the lumen. The basement membrane is prominent and hyalin in appearance. The subepithelial layer is thick, contains numerous round cells, eosinophil cells, and numerous capillaries. The muscle layer is strongly developed even to the bronchioles. The mucous glands are large, the acini of most are distended with mucus, and some glands contain large foci of round cells. The cartilages show numerous areas of calcification and one even of bone formation with its marrow. The bronchial arteries are thick walled. The alveoli show a moderate emphysema and in areas contain a granular precipitate and some polynuclear neutrophil cells.

The fourth case, Mr. L., is that of a young soldier, 29 years of age, who had had horse asthma for several years and who died a few minutes after an intravenous injection of horse serum. Dr. Boughton reported this case as a case of acute

fatal anaphylaxis and kindly furnished us with tissues for more detailed study.

The bronchi contain a granular precipitate in which are many mononuclear and polynuclear eosinophils and many polynuclear neutrophils. The epithelium is high and vacuolated and is thrown into deep folds which with the precipitate almost occludes the lumen of many of the bronchioles. The basement membrane is not prominent. The subepithelial layer varies in thickness and contains a few distended capillaries, many round cells and a few eosinophils. The muscle layer is well developed and in the bronchioli forms a definite ring. The mucous glands are small, the acini being small and widely separated by many round cells. The cartilages are normal in arrangement and structure. The bronchial arteries are very thick walled and some suggest the nodal arrangement in guinea-pigs described by Schultz and Jordan in their anaphylactic studies. The alveoli vary considerably, some show a marked emphysema, others are almost obliterated by fibrous tissue in which are numerous foci of round cells. Just beneath the pleural surface there are numerous small interstitial hemorrhages.

In conclusion we may state that pathological histological examination of the finer structure of the bronchi and its branches in these four cases of bronchial asthma suggests a certain parallelism between the clinical picture and the structural changes. Of the two cases developing on the infectious basis, one showed during life a well defined case of the exudative type characterized by an abundant secretion (bronchorrhea), which was one of the chief clinical symptoms associated with the paroxysmal attacks. The anatomical parallel to this picture is furnished by the striking hypertrophy of the mucous gland system of the bronchi.

The second case of infectious asthma was characterized clinically by a more or less unproductive cough which led to the attacks by bronchospasm. The chief pathological change seen in this case was the striking hypertrophy of the smooth muscle fiber system.

The third case, one of food asthma, is characterized pathologically by hypertrophy of both glandular and muscular systems, both of which played a rôle in the production of stenosis.

The last case, one of horse asthma, calls to mind the picture seen in the lungs of the guinea-pig in the

classical anaphylactic experiment, i. e., acute emphysema and marked constriction of the bronchi and bronchioles by the well developed ring muscle causing folding of the epithelium.

The irregular thickening of the walls of the pulmonary arteries reminds us of Schultz and Jordan's description of the nodal arrangement of these arteries in the guinea-pig.

May 10, 1920.

A HEALED DISSECTING ANEURYSM OF THE ABDOMINAL AORTA

WITH RUPTURE INTO THE RIGHT EXTERNAL AND LEFT INTERNAL ILIAC ARTERIES

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This aneurysm was obtained from the body of a woman, 60 years old, who was admitted to St. Luke's Hospital, March 13, 1920, to the service of Dr. Preble, and who died forty hours later. She was helpless, semiconscious and responded to questions incoherently.

She was large and obese. Her pupils were equal and active, although the right was sluggish. The deep reflexes were active and equal, but on the right side there were markedly positive Babinski, Gordon, Oppenheim and Chaddock signs. When admitted, there was no paralysis, but the day following there was a right facial paralysis. The distal portions of the lower extremities were edematous and there were numerous varices of the legs. The systolic blood pressure was 230 mm., the diastolic 140. The peripheral arteries were hard, and through the flaccid abdominal wall the aorta and common iliac arteries could be palpated easily. Along the course of each common iliac artery there was a nodular cylindrical pulsating mass about the size of a walnut. With the appearance of the right facial paralysis, the patient lapsed into deep coma, with incontinence of urine and feces. The spinal fluid was

bloody. The urine contained albumin, sugar, and occasional leukocytes; the blood 26.6 mg. of urea nitrogen, 50.8 mg. of total nonprotein nitrogen, 2.52 mg. of creatinin, and 6.33 mg. of uric acid per 100 c.c. of blood. The Wassermann test on both blood and spinal fluid was negative. A cerebral hemorrhage was diagnosed.

Postmortem, a huge spontaneous intracerebellar hemorrhage involving the central portion of the right hemisphere and extending into the left was found. The lining of the cerebral, coronary and other large arteries of the body was markedly roughened by senile sclerotic changes. There were similar changes in the aorta, and beginning just below the celiac axis was the mouth of a healed dissecting aneurysm, 1.6 cm. in diameter, directed forward and downward about the middle of the front wall of the aorta. The sac extended within the front wall of the aorta downward to the bifurcation and ended on the right side, 1.5 cm. below the bifurcation of the right common iliac artery where it emptied into the lumen of the right external iliac artery. On the left side the sac extended in front of the bifurcation of the aorta and within the wall of the left common iliac artery to end in the lumen of the left internal iliac artery, through an aperture 1 cm. in diameter. In the sac on the right side, just above the bifurcation of the aorta, there was a large, mural, red and gray thrombus, 6 by 4 cm., and several smaller gray thrombi adherent to the front wall of the aneurysmal sac.

In stained sections of the wall of the aneurysm, examined microscopically, there was an inner fibrous layer lined with scattered cells resembling endothelium.

May 10, 1920.

ON THE OCCURRENCE OF HEMOLYTIC STREPTOCOCCI IN THE STOOLS OF SCARLET FEVER PATIENTS*

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Hemolytic streptococci are known to occur frequently in the throats of scarlet fever patients, but there has been some question as to whether they appear in the stools. A systematic study of the stools from scarlet fever patients was undertaken to determine the presence and relative numbers of hemolytic streptococci.

The total number of stools examined was 309, in thirty-seven of which (12 per cent.) hemolytic streptococci were isolated. The stools were collected from eighty-five patients with scarlet fever, and hemolytic streptococci were isolated in twenty-six (30 per cent.) instances. From thirty-one patients only one stool examination was made, of which six (19 per cent.) showed hemolytic streptococci. To eleven patients a cathartic was administered and several stools obtained the same day. In three instances (18 per cent.) hemolytic streptococci were isolated.

The number of colonies of hemolytic streptococci on the plates on which they were noted was variable, usually six to ten out of 200 to 300 colonies of all types. Agglutination and opsonic tests were made, using blood from a sheep injected with a hemolytic streptococcus, isolated early in the course of a case of scarlet fever. Of eleven strains, six were opsonified or agglutinated by the immune serum.

Hemolytic streptococci were noted in the stools of scarlet fever patients. They were found at irregular intervals, with no definite relation to the age of the patient, character of the stool, duration or intensity of

* A full report of this work appeared in the Journal for Infectious Diseases, October, 1920, p. 363.

the illness. The number of colonies was small in comparison to those of other organisms, but when it is considered that only one loopful of the stool was studied, it seems probable that hemolytic streptococci occur perhaps more frequently than the above figures would indicate.

May 10, 1920.

THE PRECIPITIN INDEX OF THE CEREBROSPINAL FLUID WITH ANTI-HUMAN SERUM

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Qualitative and quantitative tests for the protein content of the cerebrospinal fluid came into use shortly after Quincke made examination of the fluid possible by the introduction of spinal puncture. At first the interest centered on the normal protein content; later, pathological fluids aroused greater interest, particularly after an increase in the cell count was found in certain conditions, notably, dementia paralytica. The protein content of normal fluids was ascertained to be about 0.033 per cent., varying between 0.02 per cent. and 0.035 per cent.[1] These data were obtained by complicated Kjeldahl analyses and by the use of Esbach's reagent. Zaboziecki [2] attempted to formulate a quantitative clinical method by superimposing varying dilutions of fluid on concentrated nitric acid and observing the ring formation. Nissl [3] previously tried to solve the problem by the introduction of a modified Esbach tube, Esbach's reagent being used as precipitant. These earlier methods were soon abandoned as they were too complicated, and the modern globulin tests introduced.

1. Plaut, Rehm, Schottmüller: Leitfaden zur Untersuchung der Zerebrospinalflüssigkeit, 1913.
2. Monatschr. f. Psychiat. u. Neurol., 1919.
3. Centralbl. f. Nervenheilk. u. Psychiat., 1904, 27, p. 225.

Nonne and Apelt [4] used a saturated solution of ammonium sulphate for precipitation. This two-phased reaction is still in use, though partially superseded by the Ross-Jones ring test,[5] which consists in superimposing cerebrospinal fluid on a saturated ammonium sulphate solution. Pandy [6] devised a more sensitive globulin reaction, only three drops of fluid being necessary by dropping the fluid through a saturated aqueous solution of phenol, a distinct cloud formation resulting in the case of pathological fluids. Noguchi [7] described another globulin test dependent on precipitation when butyric acid is boiled with cerebrospinal fluid. It is customary to denote the amount of reaction obtained by the Ross-Jones, Pandy or Noguchi tests in subjective terms of one, two and three plus. Different pathological processes respond differently to alkaloidal precipitants, such as sulphosalicylic acid, and to metalic precipitants, such as mercuric chlorid, and Levinson [8] concludes that these precipitants do not bear any quantitative relation to the amount of protein present in the cerebrospinal fluid. Thus, with the possible exception of the Kjeldahl and Esbach determinations, we have no accurate method of determining the total protein content, but because of their complexity these methods cannot be applied clinically. The variation in the mixture of globulins and albumins in pathological fluids demand a procedure that will give an index of the total amount of protein present. The ordinary precipitin test for human protein may be of some value from this point of view, and accordingly we have made certain observations, the results of which seem to be of some interest.

Antihuman rabbit or chicken serum, prepared in the usual manner, has been used to determine the highest dilution of cerebrospinal fluid that would give a distinct precipitate by the ring or contact method, after one hour at room temperature. By using very small tubes the amount of fluid required is insignificant. Particu-

4. Arch. f. Psychiat., 1905, 43, p. 433.
5. Brit. Med. Jour., 1916, 1, p. 444.
6. Neurol. Zentralbl., 1910, 29, p. 915.
7. Serum Diagnosis of Syphilis, 1910.
8. Cerebrospinal Fluid, 1918.

lar care was taken to prevent admixture with blood when the fluid was drawn, and only fluids found to be free from blood corpuscles have been tested. The cell counts were made with high power, after staining in the usual way with methyl violet. This report covers 100 cases in the Cook County Psychopathic Hospital. In order to simplify discussion, the results are recorded as if obtained with the same antihuman serum, titer 1,000, when tested with human blood, and we designate as the precipitin index of cerebrospinal fluid the highest dilution of fluid with normal salt solution giving a distinct precipitate under the exact circumstances just described. In the actual tests, antihuman serums of different titers were used, but as stated all results have been reduced to the same standard. We divide the cases from which fluids were obtained into three fairly distinct groups.

The first group, Table 1, includes fifty-three cases that gave no reaction with the usual tests for globulin, including twenty-seven cases of dementia praecox, some cases of toxic psychoses, a few mild organic diseases of the brain and a few mental diseases other than those mentioned. All the patients were in good physical health. Judging from the results of the usual tests, we are dealing here with normal cerebrospinal fluids. As seen in Table 1, the precipitin index varies from 1.2 to 8.0, the average being 3.7, if we disregard Case 20. In the case of this fluid, we believe that in spite of the fact that no erythrocytes were present, serum proteins must have affected the results. In using the colloidal gold test, it is a matter of common experience, that serum globulin and albumin often nullify the results even if only a few red blood corpuscles are seen in the microscopic field. Therefore, a seepage of these substances into the spinal canal is possible without extensive injuries to the walls of the venous plexus. At any rate this seems a reasonable explanation of such a divergent result.

The second group, Table 2, of thirty-four cases, twenty of which are outspoken cases of general paresis, is very interesting. The precipitin index in most of these cases is higher, averaging 12.6; in all but two

cases it is above the normal average. One of these, Case 19, is unusual in that the fluid from a paretic gave a negative Wassermann reaction. The next sub-

TABLE 1.—GROUP 1

No.	Diagnosis	Cells in C.c.	Wassermann Test	Colloidal Gold Test	Ross-Jones Test	Noguchi Test	Pandy Test	Precipitin Index
1	Dementia praecox....	0	0	0002110000	0	0	0	4.0
2	Dementia praecox....	1	0	0000000000	0	0	0	3.3
3	Dementia praecox....	1	0	0000000000	0	0	0	3.8
4	Dementia praecox....	2	0	0000000000	0	0	0	1.5
5	Dementia praecox....	0	0	0000000000	0	0	0	1.5
6	Dementia praecox....	2	0	0000000000	0	0	0	2.9
7	Dementia praecox....	6	0	0000000000	0	0	0	5.6
8	Dementia praecox....	0	0	0000000000	0	0	0	4.6
9	Dementia praecox....	2	0	0000000000	0	0	0	4.6
10	Dementia praecox....	6	0	0000000000	0	0	0	4.0
11	Dementia praecox....	14	0	0000000000	0	0	0	1.6
12	Dementia praecox....	4	0	0000000000	0	0	0	1.2
13	Dementia praecox....	1	0	0000000000	0	0	0	8.0
14	Dementia praecox....	2	0	0000000000	0	0	0	4.8
15	Dementia praecox....	1	0	0000000000	0	0	0	4.0
16	Dementia praecox....	0	0	0000000000	0	0	0	4.8
17	Dementia praecox....	4	0	0000000000	0	0	0	4.8
18	Dementia praecox....	0	0	0000000000	0	0	0	4.8
19	Dementia praecox....	0	0	0000000000	0	0	0	3.2
20	Dementia praecox....	2	0	0000000000	0	0	0	19.2
21	Dementia praecox....	0	0	0000000000	0	0	0	4.8
22	Dementia praecox....	4	0	0000000000	0	0	0	4.0
23	Dementia praecox....	2	0	0000000000	0	0	0	4.0
24	Dementia praecox....	0	0	0000000000	0	0	0	1.6
25	Dementia praecox....	3	0	0000000000	0	0	0	8.0
26	Dementia praecox....	1	0	0000000000	0	0	0	3.2
27	Dementia praecox....	4	0	0000000000	0	0	0	1.6
28	Chronic alcoholism...	1	0	1112210000	0	0	0	1.7
29	Chronic alcoholism...	11	0	0000000000	0	0	0	5.9
30	Chronic alcoholism...	5	0	0000000000	0	0	0	5.9
31	Chronic alcoholism...	2	0	0000000000	0	0	0	1.2
32	Chronic alcoholism...	2	0	0000000000	0	0	0	4.8
33	Chronic alcoholism...	4	0	0000000000	0	0	0	4.0
34	Chronic alcoholism...	6	0	0000000000	0	0	0	2.4
35	Chronic alcoholism...	4	0	0000000000	0	0	0	6.4
36	Senile dementia.....	8	0	0001210000	0	0	0	1.2
37	Senile dementia.....	3	0	0000110000	0	0	0	8.0
38	Senile dementia.....	6	0	0000000000	0	0	0	4.0
39	Senile dementia.....	6	0	0000000000	0	0	0	4.0
40	Senile dementia.....	5	0	0000000000	0	0	0	2.4
41	Senile dementia.....	0	0	0000000000	0	0	0	2.4
42	Senile dementia.....	6	0	0000000000	0	0	0	3.2
43	Senile dementia.....	5	0	0000000000	0	0	0	2.4
44	Neurasthenia dept...	5	0	0001110000	0	0	0	2.5
45	Neurasthenia dept...	0	0	0000000000	0	0	0	2.4
46	Undiagnosed.....	10	0	0000000000	0	0	0	5.8
47	Undiagnosed.....	2	0	0000000000	0	0	0	1.5
48	Hypo-mania.....	4	0	0000011000	0	0	0	4.8
49	Mentally defective....	0	0	0000000000	0	0	0	1.5
50	Toxic psychosis.....	1	0	0011100000	0	0	0	3.2
51	Skull fracture.....	12	0	0000000000	0	0	0	3.2
52	No findings.....	4	0	0000000000	0	0	0	4.9
53	No findings.....	0	0	0000000000	0	0	0	2.4

group of six cases of cerebrospinal lues gives values that are about normal, averaging 3.6. The last six six cases, a mixed group, also show normal indexes averaging 2.1. The precipitin index consequently appears as being consistently high in general paresis. The cases in this group were grouped together because

TABLE 2.—GROUP 2

No.	Diagnosis	Cells in C.c.	Wassermann Test	Colloidal Gold Test	Ross-Jones Test	Noguchi Test	Pandy Test	Precipitin Index
1	General paresis....	432	4+	1133444110	4+	3+	4+	32.0
2	General paresis....	50	4+	5555555321	2+	+	3+	8.0
3	General paresis....	23	4+	5555553210	2+	+	2+	4.0
4	General paresis....	8	4+	5555555421	2+	2+	3+	16.0
5	General paresis....	78	4+	5555554310	2+	+	2+	5.0
6	General paresis....	60	4+	5555554321	2+	+	3+	12.5
7	General paresis....	36	2+	5555433200	+	+	+	5.0
8	General paresis....	50	3+	5555544310	2+	+	2+	5.9
9	Taboparesis.....	24	+	0001123100	+	+	+	9.0
10	General paresis....	16	2+	5555554432	2+	2+	2+	11.8
11	General paresis....	62	4+	5555554320	2+	2+	2+	16.0
12	Tobaparesis.....	32	4+	5555554210	2+	2+	2+	19.2
13	General paresis....	20	3+	5555443210	2+	2+	2+	9.6
14	General paresis....	44	4+	5555555542	2+	2+	2+	40.4
15	General paresis....	2	2+	5554433210	0	0	(+)	9.6
16	General paresis....	22	3+	5555543110	2+	+	2+	19.2
17	General paresis....	30	4+	5555542000	2+	2+	2+	19.2
18	Taboparesis.....	24	4+	5555555430	2+	2+	2+	9.6
19	Taboparesis.....	62	3+	5555433210	2+	2+	2+	19.2
20	General paresis....	16	0	5554432100	2+	2+	2+	1.6
21	General paresis....	36	4+	5555555420	2+	2+	2+	4.8
22	General paresis....	40	4+	5555554310	2+	2+	2+	2.4
23	Cerebrospinal lues	12	0	0000121000	+	+	+	5.9
24	Cerebrospinal lues	20	3+	0000000000	+	+	+	2.9
25	Cerebrospinal lues	15	+	0001210000	+	+	+	1.5
26	Cerebrospinal lues	14	0	0013553210	+	+	+	4.8
27	Cerebrospinal lues	24	0	0013554310	2+	2+	2+	3.2
28	Cerebrospinal lues	8	4+	0012321100	+	+	+	3.2
29	Dementia praecox	14	0	0000000000	+	+	+	2.4
30	Dementia praecox	8	0	0000000000	+	+	+	4.8
31	Senile dementia...	15	0	0000211000	+	+	+	4.0
32	Organic brain disease.....	32	0	0000110000	+	+	+	2.4
33	Mentally defective	38	0	0000000000	+	+	+	1.5
34	Neurasthenic depression.....	16	0	0000000000	+	+	+	2.3

the globulin tests were positive, but the precipitin index is high in general paresis only. It is of interest to note that the precipitin index may be low in the presence of strongly positive globulin tests as usually recorded and high when weakly positive globulin reactions are obtained.

The last group is one (Table 3) in which traces of globulin were found by the usual tests. Epileptic cerebrospinal fluid appears to have a rather high index, the average for five fluids being 5.3, which is above normal. It has been noticed that the Pandy reaction, the most sensitive of all globulin tests, often gives a slightly positive result with the cerebrospinal fluid of epilepsy.[9] While more work must be done before definite conclusions can be drawn, the point is of interest. The average for the whole group is 3.3 In Case 6, an unusual result was obtained, possibly due to error. The lack of balance between the precipitin index and the usual globulin tests is again noticeable.

TABLE 3.—GROUP 3

No.	Diagnosis	Cells in C.c.	Wassermann Test	Colloidal Gold Test	Ross-Jones Test	Noguchi Test	Pandy Test	Precipitin Index
1	Epilepsy.....	0	0	0001100000	(+)	0	+	6.0
2	Epilepsy.....	0	0	0000110000	0	0	(+)	6.3
3	Epileptic psychosis...	4	0	0000110000	0	0	(+)	1.6
4	Epilepsy.....	1	0	3332100000	0	0	(+)	4.8
5	Traumatic epilepsy...	8	0	0000000000	0	0	(+)	8.0
6	Senile dementia.....	7	0	0000012000	0	0	(+)	16.8
7	Senile dementia.....	6	0	0000000000	0	0	(+)	4.0
8	Senile dementia.....	2	0	0000122100	0	0	(+)	2.4
9	Dementia praecox....	2	0	0000000000	0	0	(+)	4.0
10	Dementia praecox....	2	0	0000000000	0	0	(+)	6.4
11	Dementia praecox....	3	0	0000000000	0	0	(+)	4.8
12	Dementia praecox....	1	0	0000000000	0	0	(+)	1.6
13	Mentally defective....	0	0	0011000000	(+)	0	+	8.0

Naturally, this test for protein, including globulin and albumins, will give a general idea of the total amount present. This may be determined, as we have done, by noting the highest dilution of spinal fluid which still shows a precipitate. It may also be obtained by weighing the amount of precipitate obtained by mixing antihuman serum of a given titer with cerebrospinal fluid. The method has certain apparent difficulties which should be noted. It is necessary to keep a serum of the right strength on hand, and to test the strength of the serum from time to time for its pre-

9. Neymann and Brush: Arch. of Int. Med., 1918. Vol. xxii p. 245.

cipitin titer. This is a minor difficulty, since such sera change their titer very slowly, provided they have not been contaminated. The other difficulty is that of keeping the cerebrospinal fluid absolutely free from blood. Careful microscopic examination will prevent trouble in this direction. It is manifest that inflammatory conditions of the meninges will give a very high precipitin index. We cannot yet judge the clinical value of this test. However, our results appear to indicate the desirability of further investigation, particularly with epileptic spinal fluids.

May 10, 1920.

MAXIMILIAN JOSEPH HERZOG

TRANSACTIONS OF THE
CHICAGO PATHOLOGICAL SOCIETY

VOL. XI. MARCH 1, 1921. NO. 4

THE LIFE AND WORKS OF MAXIMILIAN JOSEPH HERZOG

CHARLES S. BACON

Although it is more than two years since the death of our former colleague and friend, his memory remains fresh and distinct with those of us who knew him well. His strong, impressive personality could not be neglected during his lifetime and is in no danger of being forgotten by his former associates. Our Society, however, should possess a sketch, or outline, of his work for the benefit of those who come after him as well as for the gratification of those who knew him intimately.

I was fortunate in knowing Dr. Herzog quite well, meeting him shortly after his arrival in Chicago and following his work with much interest from that time till his death. In company with all who enjoyed the privilege of a closer acquaintance I can recall him as a charming companion; witty, kindly and always welcome in every circle. As a student and research worker he was fearless, inventive, indefatigable. He possessed a clear, attractive literary style that gave his writings a charm not very common to medical writings. He was by nature a pedagogue and brought to the class room a combination of teacher and research student that formed the ideal instructor. At one time a newspaper writer and editor, he retained a lively interest in social affairs and politics. His love for music and art and his extensive travels gave him a wide horizon and made him, with his universal sympathies, a world citizen.

He was born in Frankfort-on-the-Main, Sept. 17, 1858. His father could not afford to give him a university education. After the usual thorough foundation course of the lower schools, Max entered the famous bank of Speyer and Co., in Frankfort, where he worked till he reached the age of 20 years. By this time he had developed a great interest in the natural sciences and decided that he could never be contented with a business career. With the savings from his work as a bank clerk he spent the next three years in the universities of Giessen, Strassburg, and Marburg as a student of biology, chemistry and physics. He also took courses in philosophy in which he got a thorough foundation which served him well in his later life. He also became a great reader and student of German and French literature. These courses in literature turned out to be very valuable preparation for his subsequent work as journalist.

Although he was offered a relatively good position in the bank on the completion of his university course, his enterprising spirit was not satisfied with the outlook of a business career and he came to the United States in 1882. He at once applied for naturalization and received his final papers in the probate court of Hamilton County, Cincinnati, Ohio, in 1887. From 1882 to 1890 he was engaged as newspaper writer (reporter, city editor, managing editor), on the German daily press, one year in St. Louis, and the remainder of the time in Cincinnati. He also acquired recognition as an acute and competent critic of art and music and naturally became acquainted with many of the leading men of the country.

At this time he met his future wife, Seraphina Enrau, an actress well known in Europe and this country, whom he married in Chicago in 1894. The mutual understanding, appreciation and sympathy between husband and wife made this a happy union.

In spite of his success as a journalist, Herzog's inclination to and love for the natural sciences were not satisfied and he decided to choose medicine for his life work. From 1885 to 1890, while still engaged

in his newspaper work, he studied medicine in the Medical College of Ohio, Cincinnati, and graduated with honors in 1890. He then chose as his specialty, otology, rhinology and laryngology and spent the next two years in postgraduate studies in Europe in the universities of Wuerzberg, Munich, Leipzig, Berlin and Vienna. In December, 1892, he returned to the United States and practiced medicine in Cincinnati until the summer of 1894. During this period he was a member of the medical staff of the German Hospital in Cincinnati.

In 1894 he came to Chicago and started to build up a practice in his specialty. In this he was not immediately successful. He was naturally a student and investigator and neither satisfied with nor successful in the routine work of practice. Much of his spare time, of which he had an abundance, was given to the study of the pathology of the nose and ear, which resulted in the first eleven of his published papers. When in 1896 there was a chance to devote himself to pathology and bacteriology as professor in the Chicago Policlinic he accepted it with eagerness and thus found the life work suited to his genius and satisfying his desires. This position he secured through his true friend, the late Walter S. Christopher, to whom he remained devotedly grateful during his life.

He remained with the Policlinic for seven years, till 1903. During this time he had good opportunities for work which he used to the utmost. The connection was mutually advantageous, for the school profited by the presence of a real worker. All of the operative material of Professor Henrotin and his colleagues in the gynecological and surgical departments was worked up by Herzog, who published at this time many of his important papers on embryology and obstetrical and gynecological pathology. At this time the functions and pathology of the pancreas began to attract considerable notice and Herzog made his contributions to the subject. The whole of the specialties were included in his work. Considering the character of the work and the fact that it was done almost without help we may all agree that it was productive and valuable.

Besides his work in the Policlinic he assumed also the duties of pathologist to the German Hospital and to the Maurice Porter Hospital for Children.

In 1903, still driven by his enterprising spirit and eager for new fields, Herzog left Chicago and became pathologist in the Bureau of Science, Manila, P. I. Here he had the opportunity to study tropical diseases, then a little known field to American physicians. Numerous papers on the bacteriology, morbid anatomy and pathology of the plague soon appeared in the publications of the bureau and in medical journals. In 1906 he was ordered by the Philippine government to Japan to study beri-beri, the results of which appeared in the Philippine Journal of Science in the same year and in Osler's Modern Medicine in 1907.

Upon his return to Chicago in 1906 he added to his field of study and research that of comparative pathology. His return coincided with the interest aroused in the stockyard's sanitation and he was appointed one of the experts of the Illinois Manufacturers' Association and the Chicago Commercial Club's Stockyards Investigation Committee. At the same time he became professor and bacteriologist in the Chicago Veterinary College, which position he held till 1913. As fruits of his work in this field there appeared in veterinary medical publications several articles, including descriptive articles on tumors in domestic animals and a paper on Trypanosomes and diseases caused by them, which appeared in the Proceedings of the American Veterinary Association, Philadelphia, in 1910. He also began the preparation of his really monumental work, a Text-Book on Comparative Pathology, which he completed shortly before his death. For the illustrations for this book, 578 in number, he spent over $5,000, a very large sum of money for him. The book was to be published by Saunders & Co., but unfortunately the publication was delayed until finally, last year, his widow withdrew the contract, hoping to secure another publisher. This hope was in vain and so this work, which would have been a credit to

American Science and a permanent monument to our deceased Fellow, lies at present in a safety vault unknown and useless.

Upon his return from the Philippine Islands he was at various times pathologist to a number of hospitals in Chicago. For three years he was pathologist to the Michael Reese Hospital and later he was on the staff of the German Hospital, Alexian Brothers Hospital and the North Chicago Hospital. He was also pathologist to the Cook County hospital and in 1914 he secured, by civil service examination, the position of Chief of the Department of Pathology. In 1912 he became Professor of Pathology and head of the Department of Pathology, Bacteriology and Hygiene in the Medical Department of the Loyola University and the next year he was made Dean of the College, which position he held till his retirement because of ill health, in 1916. In 1918 he received from the Loyola University the honorary title of LL.D. He was also a member of the state civil service medical examining board for the state institutions from 1906 to 1913. In 1916 he became medical director of the Municipal Tuberculosis Sanitarium, which position he held till his death.

During the last twelve years of his life, besides the work of comparative pathology already mentioned, and work connected with teaching and organizing in the schools and hospitals with which he was connected, he made a considerable number of other important contributions to medical science. One of the most interesting was a study of a very early embryo which he incorporated in a paper presented to the Seventh International Zoological Congress held in Boston in 1907, and later published in the *American Journal of Anatomy* in 1909, under the title "A Contribution to Our Knowledge of the Earliest of Placentation and Embryonic Development in Man." He presented this work as an exhibit to the American Medical Association at its annual meeting in 1908, and received a certificate of honor. This exhibit was

afterward presented to Harvard University. A very unique specimen of pregnancy in a uterine adenomyoma was described in a paper presented to the Chicago Medical Society in 1911. He contributed to Wm. Robertson's Textbook on Meat and Food Infection, published by Keener in 1908. He wrote a text-book, published by Lea & Febiger in 1910, on Disease-Producing Micro-Organisms. He also completed for publication a work on enzymes that had engaged his most interested attention since the beginning of his medical studies. His studies in biological and physiological chemistry early led to the development of a theory of enzymes which he presented in abstract to the Chicago Medical Society shortly after his arrival in Chicago in 1896. This abstract was published in the *Chicago Medical Record*. According to his theory enzymes are not, as heretofore believed, chemical compounds in the ordinary sense of the word but very minute live organisms, possessing all the properties of live organisms, namely, the power of assimilation, metabolism, growth and reproduction. They are in fact the real basis of life, the true elementary organisms of all that we call life. Years of investigation only served to justify his belief in his theory and finally he was able to arrange for the publication of his material very shortly before his death. This article has just been published as a monograph by the Chicago Municipal Sanatorium under the title "A Contribution to the Study of the Nature of Enzymes."

He was a member of many societies, including the Chicago Medical Society, the Illinois Medical Society, American Medical Association, the Chicago German Medical Society, the Chicago Pathological Society, the Society of Medical History, etc. He was president of the Chicago Pathological Society in 1901 and 1902, and gave his president's address on Rudolph Virchow. He was twice president of the Chicago German Medical Society. He was also a Fellow of the American Association of Pathology, American Society of Bacteriologists, American Association for Cancer Research,

American Association of Anatomists, American Microscopical Society, American Society of Tropical Medicine and the American Association for the Advancement of Science. He was also first lieutenant of the Medical Reserve Corps of the U. S. Army.

Three or four years before his death, while making a postmortem examination in the County Hospital he received a wound of a finger which led to a serious infection that nearly proved fatal. This was the beginning of a sickness from which he suffered much and from which he never recovered. He died in his rooms in the Tuberculosis Sanitarium, September, 1918. The postmortem examination made by Dr. Hektoen confirmed the anatomical diagnosis made by Herzog himself before his death. There were found chronic nephritis, hypertrophy of the heart and fibrous myocarditis, sclerosis of coronary arteries and aorta, old pleural tuberculosis and fibrocaseous tuberculosis of the peribronchial nodes; chronic cholecystitis with calculi, fibrous pancreatitis, etc.

In reviewing the life work of this man, and recalling his writings, I am impressed anew with his magnificent talents and capabilities. Knowing the hindrances of all kinds under which he labored I am confirmed in the belief that only a rare mind could have done his work. Under better auspices, perhaps he could have done more. He was cut off in the midst of his work. It is to be hoped that some way may be found to secure the publication of the Text-Book on Comparative Pathology. We may well be proud of his achievements and glad that he was one of our members. His energy and his intellectual honesty, his genial and kindly spirit remain to us a stimulus and encouragement.

Nov. 8, 1920.

HEMOLYTIC STREPTOCOCCI OF THE APPENDIX VERMIFORMIS

ADOLPH KRAFT

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The significance of hemolytic streptococci in the etiology of appendicitis is not well known. In view of the foregoing fact, an investigation of this lesion was undertaken to determine the frequency with which hemolytic streptococci are found in normal, acute and chronic appendices; and to determine if possible the rôle they play as a primary etiological factor of appendicitis. The work consisted in the collection of material, isolation of various strains of hemolytic streptococci and their classification, animal inoculation, and a study of the probable route of infection.

The appendices were gathered from various clinics, and while still free from contamination, they were examined within a few hours after the operation. Gross examination, smears of lumen contents and mucosa, and bacterial culture of mucosa and wall were made. Care was taken to use only sterile instruments and culture material in this work. Special attention was given to the blood agar plates and beef broth cultures. The blood agar plates were examined for colony growth with special reference to hemolysis, size, shape, color, elevation, pigmentation, moisture, predominance, and variety of colonies. Only those colonies that gave a distinct hemolysis about a small pin-point grayish slightly elevated growth, and that on staining showed Gram positive cocci growing in chains or diplococci form, were tabulated as hemolytic streptococci. Later confirmatory tests were made and the organisms grouped in accordance with Holman's scheme. All nonhemolytic streptococci producing a green halo were classed tentatively as streptococcus viridans.

The several strains of hemolytic streptococci isolated were pathogenic for rabbits. There was no elective

affinity of these strains for the appendix; it was difficult to determine definitely what the route of infection may have been.

Hemolytic streptococci were found in two of forty-eight normal appendices; approximately in 4.17 per cent.

Hemolytic streptococci were found in four of seventy-seven pathologic appendices; approximately in 5.2 per cent.

In the pathologic series they were found in the acute cases only, approximately in 7.65 per cent. They were not recovered from the chronically inflamed appendices.

When hemolytic streptococci occurred in pathologic appendices they were present in large numbers and in practically pure culture; while when found in the normal appendices they were present in only few numbers.

Two types of these organisms appeared; according to Holman's scheme they were: Streptococcus infrequens (5 strains) and Streptococcus hemolyticus II (1 strain).

Hemolytic streptococci apparently do not play an important rôle in the production of appendicitis; however, when they do occur in pathologic appendices, they usually predominate and appear to be the direct etiologic agent.

Nov. 8, 1920.

THE RELATION OF MULTIPLE VASCULAR TUMORS OF BONE TO MYELOMA *

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From time to time articles have appeared discussing vascular tumors arising in the bones, which have presented peculiarities resulting in their designation variously as pulsating sarcoma, bone aneurysms, hemangiosarcoma and hemangioendothelioma, a variety of

* The full details are published in Archives of Surgery, 1921, ii, 435.

terms which indicate either that several different pathologic conditions may present similar characters, or that a single condition presents different features at different times and places. I have had occasion to study a case belonging to the group of vascular tumors of bone, which has seemed to explain certain features of the striking and peculiar angiomatous character of these growths.

The subject was a Lithuanian laborer, 45 years old, who presented the clinical picture of malignant neoplasm of the vertebral column with pathologic fracture and compression of the spinal cord. Necropsy disclosed growths in the 3rd, 10th, 11th and 12th dorsal vertebrae, with involvement of the 11th and 12th ribs, and neoplastic infiltration of the adjacent tissue, as well as two isolated subpleural nodules. The extraosseous tumor tissue was pale and microscopically showed the features of multiple myeloma of the myeloblastic type. The tumors within the bones were soft, dark red, gelatinous masses, often jelly-like. These showed little or no evidence of myelomatous structure, but consisted of wide blood spaces, lined with cuboidal endothelium, often in several layers. Between the blood channels were embryonal connective tissue elements, often of myxomatous character or of embryonal cartilage cells. These bone tumors, therefore, correspond to the growths that have often been interpreted as multiple endothelioma of bone. In this case, and probably in many of the others thus diagnosed, the process is really multiple myelomatosis, with hemorrhagic necrosis of the tumor tissue within the bones. The resulting blood clots become organized, but as the new-formed tissue cannot contract because of its intimate connection to the adjacent bone the blood channels remain patulous and of embryonic character, thus simulating hemangioendothelioma.

Nov. 8, 1920.

CHRONIC DISSECTING SUPPURATION OF THE BLADDER WALL SECONDARY TO A SMALL ABSCESS IN THE HYPERTROPHIED MIDDLE LOBE OF THE PROSTATE GLAND

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Suppuration of the deeper layers of the bladder wall, while unusual, is described by Delafield and Prudden [1] as a result of extension from a suppurative process beginning in the mucous membrane of the bladder. According to Kaufmann,[2] cystitis may be the result of ascending infection through the urethra, descending through the ureters, direct extension from pelvic inflammations outside the bladder, and hematogenous infection in acute infectious diseases and septicemias. The same author [3] states that abscesses of the prostate gland may perforate into the urethra, perineum, rectum and peritoneum. In some examination of medical literature, but by no means exhaustive, I have not found accounts of dissecting suppuration of the bladder wall secondary to abscesses of the prostate gland, such as the following contains.

A man, found dead at a lodging house, had been sick for five months, and, so far as known, was not under a doctor's care at the time of death. At the postmortem examination (Dr. E. R. LeCount) the following were the principal points in the anatomic diagnosis: extensive bilateral pyelonephritis; suppurative cystitis and perivesiculitis; generalized serofibrinopurulent peritonitis; marked hypertrophy of the middle lobe of the prostate gland. Pus from the left kidney and peritoneal cavity yielded streptococcus pyogenes on culture.

The empty bladder is enlarged, measuring 9 cm. up and down, 5 front to back and 8 transversely. The wall is thick and boggy. There are a thin layer of fibrin and a few

1. A Text-Book of Pathology, Delafield and Prudden, 1919, 11th Ed., pp. 899-900.
2. Kaufmann: Specielle Pathologische Anatomie, 1911, 6th Ed., Vol. 2, pp. 880-884.
3. Kaufmann, l.c., p. 934.

petechial hemorrhages on the vertex. The mucosa is gray, pale and slightly roughened. There are marked trabeculation and multiple diverticula of the mucous membrane, the orifices of the diverticula averaging 2 mm. in diameter. Thick, gray pus can be squeezed from these and from numerous places in the mucous membrane of the body. The trigone is smooth and the ureteral orifices slitlike and gray. The torus interuretericus is 4 cm. long, 0.5 cm. wide and is placed 2.5 cm. above the upper limit of the enlarged prostatic middle lobe. Beginning on a horizontal line 1 cm. above this ridge, there is a suppurative dissection of the bladder wall included between lines dropped vertically through the ureteral orifices; the affected region describes an arc over the summit of the bladder, extends down the pubic surface to the line of junction of bladder and prostate, while its lateral margins are slightly convex outward. The entire region contains gray-green pus between the hypertrophied muscular fibers. The lateral walls of the bladder are not so affected over a slightly pouched region 3 cm. in diameter. The bladder wall is 1.5 cm., 3 cm. and 1 cm. thick at the summit, pubic and basic portions, respectively. The prostate gland is 3.5 cm. long, 4 cm. broad and thick, being slightly enlarged in the anteroposterior diameter. It is firm, gray-pink and there is a slight, diffuse enlargement of the lateral lobes causing an inward bulging of the lateral walls of the prostatic urethra. The middle lobe is markedly enlarged, forming a nodular obstruction at the neck of the bladder; it projects upward into the bladder, measuring 2 cm. vertically and front to back and 4 cm transversely; on its upper surface in the median line is a longitudinal furrow 0.2 cm. deep and 1 cm. wide, continuous below with the urethra. On transverse sections of the middle lobe there is seen a small, oval abscess 1 mm. in front of the posterior surface of the lobe, the same distance to the left of the midline and 10 mm. below the urethral floor; the abscess is 4 mm. up and down, 3 mm. side to side and front to back and contains gray-green pus. Elsewhere the prostate is gray, firm and smooth and only a small amount of clear secretion can be expressed from its ducts. There are no changes of the penis, vasa deferentia, seminal vesicles, ejaculatory ducts and rectum and only slight senile sclerosis of the abdominal aorta. There is extensive bilateral pyelonephritis and dilatation and hypertrophy of both ureters.

In sections of the middle lobe of the prostate gland there are numerous acini with a fibromuscular stroma, in all fields, varying from 10 to 50 in an individual low power field and from $\frac{1}{25}$ to $\frac{1}{6}$ low power field diameters across. (Leitz No. 4 ocular and No. 3 objective). They are lined by a single layer of cuboidal epithelium with basal nuclei and contain pale-

pink, granular material. In the supporting stroma the smooth muscle is about five times as plentiful as the fibrous tissue. There are also two irregularly shaped, sharply outlined regions partially filled with faint pink, granular, necrotic tissue, the whole encircled by a layer of fibromuscular tissue. The larger of these is about 2.5 low power field diameters in its greatest measurement, the small 1.5. In the latter, lying within and against the wall, there is a large mass of densely packed polymorphonuclear leukocytes occupying almost one half a low power field. The stroma for 1/20 a low power field diameter adjacent to this mass is infiltrated with wandering cells, the majority plasma cells, while in places about the periphery of the other region are similar infiltrations. In another part of the section are two similar, smaller, interconnecting regions about which the stroma is also infiltrated with wandering cells. With phosphotungstic acid hematoxylin the granular, necrotic material stains pink. Stained by the Gram-Weigert method for bacteria in tissues, no organisms are found in this place.

In similar sections from the front wall of the body of the bladder, in the middle or circular layer of muscle there is a region 3 low power field diameters long and 1/3 in its greatest width, which contains densely packed wandering cells, the majority plasma cells resting in a wide-meshed network of white, fibrous tissue. Fibroblasts are abundant in this region and no muscle fibers can be seen. The region extends for the greater part of its length along the outside of a blood vessel which has been cut longitudinally, while at one point there is a collection of cells within the lumen of the vessel and apparently adherent to the lining. In one densely packed oil immersion field there are 40 polymorphonuclear leukocytes and about 30 small lymphocytes, 4 fibroblasts and 400 plasma cells. For 1/8 of a low power field diameter to each side of this region the muscle stains less intensely, while its cells are in many places fragmented and their nuclei are not visible. Scattered throughout the remainder of the middle and outer muscular layers and the fibrous coat are irregularly shaped collections of cells, predominantly plasma in type, with necrosis of the fixed tissue in the immediate vicinity. There are a few, scattered wandering cells in the tunica propria of the mucosa, while the submucosa is apparently unchanged. The phosphotungstic acid hematoxylin stain does not demonstrate any marked increase in the white fibrous tissue and the bladder lesion appears younger than that of the prostate. Sections stained by Gram-Weigert's method for bacteria contain many small diplococci and short, narrow bacilli, both intracellular and extracellular, in the regions of cellular infiltration.

The lesions described concern a chronic, dissecting suppuration of the bladder wall and a small chronic abscess in the hypertrophied middle lobe of the prostate gland. Both conditions are unusual. Although there is a purulent infiltration of the mucous membrane of the bladder, the changes are not those ordinarily produced by a suppuration beginning in the mucous membrane and extending to the muscle. Grossly and microscopically the mucosa is intact and its involvement mild while the submucosa and inner layer of muscle are apparently uninvolved. It is thought the dissection of the middle and outer layers of bladder muscle in this case is a separate infection from that of the mucous membrane. Because the small abscess of the prostate is older than the process of the bladder wall and the middle layer of bladder musculature is continuous with that of the prostate,[4] and because of the proximity of the lesion in the bladder wall to the junction of prostate and bladder, it is believed the suppuration in the bladder wall is secondary to the abscess in the prostate. The usual abscesses of the prostate are multiple in the course of chronic gonorrhea.[5] The absence of any signs of chronic gonorrhea, either in the prostate, urethra or seminal vesicles, and the presence of many foci of suppuration in the bladder mucosa and kidneys, would favor a hematogenous infection of the prostate.

Nov. 8, 1920.

4. Gray's Anatomy, 1910, 8th Ed., p. 1365.
5. Wilson and McGrath: Surgery, Gynecology and Obstetrics, 1911, Vol. 13, p. 656.

A HEART WITH A CONGENITAL PATENT INTERVENTRICULAR SEPTUM

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ELIZABETH PAULINE WOLF

In the course of a necropsy performed on a man who had died of acute influenzal pneumonia a rare heart defect was discovered, a patent interventricular septum in an otherwise normal heart.

We have been able to find only seventeen similar cases in the literature on heart defects. Cases in which this defect was combined with other malformations are numerous and no attempt has been made to enumerate or classify them.

Eight cases were reported in "The Transactions of the Pathological Society of London."

1. Jenner, in 1849, reported the case of a man aged 18 years. This heart showed an oblique opening the size of a crow-quill between the right and left ventricles through a fixed curtain formed by the tricuspid valves. The orifice on the left side was situated a little below the aortic valves at the fossa and was about four lines in diameter. The edges of the aperture projected slightly on the left side and were indurated, white and opaque. On holding the heart up to the light there were two or three places where the septum ventriculorum was very thin, only two layers of lining being present.

2. Peacock, in 1854, reported the case of a female infant; there were two openings in the septum so that the ventricles communicated. The aorta arose from the left ventricle, but near the orifice there were two openings in the septum ventriculorum by which the ventricles communicated and these openings were much larger on the left than on the right side. Both openings led into the right ventricle behind the auricular-ventricular valves. The largest had a circumference of six lines.

3. Hillier reported, in 1859, the case of a female child 2 years old. There was an opening large enough to admit a good sized pea in the upper part of the septum leading from the right to the left ventricle. The tricuspid valve consisted of two flaps which were bound to the wall of the ventricle.

4. Hilliar reported another case in 1860 of a male child 14 months old. In this case below the attached margin of one of the semilunar valves of the aorta there was a depression in the wall of the left ventricle from which extended a small hole the size of a moderate sized pinhead, leading from the left to the right ventricle.

5. Callender, in 1858, reported the case of a boy whose heart showed an irregular septal perforation, passage through being prevented by a valve-like portion of fibrin.

6. Kelly, in 1870, reported the case of a female 33 years old in whose heart the septum between the ventricles was deficient in the upper part, allowing exchange of blood between the right and left ventricles. The tricuspid valves were united above to form two cusps.

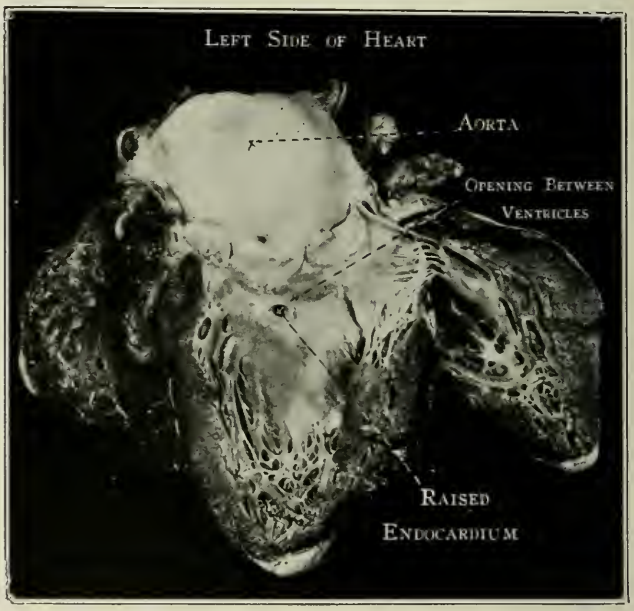

Fig. 1.—Left side of heart, showing patent septum ventriculorum.

7. Hadden's case, in 1882, was a female child of 4 months. The septum was imperfect above, the cavity admitting the middle finger.

8. Hebb, in 1897, reported the case of a female 18 years of age. There was a funnel-shaped defect in the interventricular septum admitting a goose-quill.

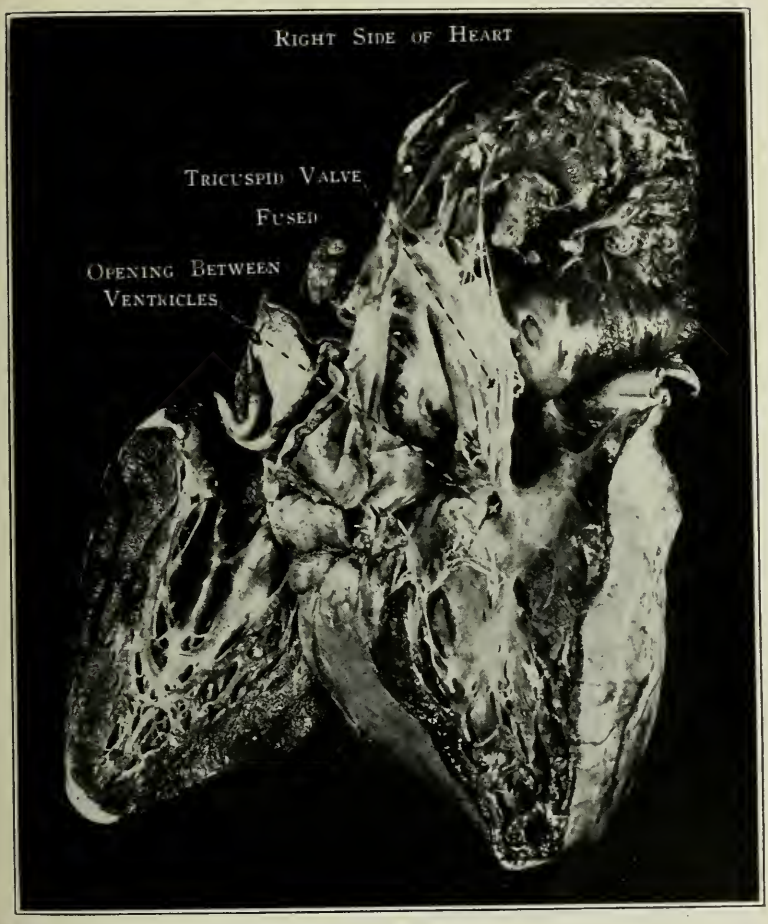

Fig. 2.—Right side of heart, showing septum ventriculorum.

9. Grüber, in "Memoirs de l'Academic de petersbourg," 1859, reported the case of a heart in which there was a fine canal between the right and left ventricles. This heart was from a man aged 36 years.

10. Rokitansky, in "Die Defects der Scheidewände des Herzens," in 1875, reported only one case of pure interventricular septum defect occurring in the heart of a man 39 years old, the opening being "the size of a strawberry." The aortic cusps were thin. All the other cases he cited were combined lesions; usually endocarditis was present and partially responsible for the defect.

11. Miller, in Virchow's Archivs, 1875, reported a case of patent septum interventriculorum in a child of 9 weeks, the defect was the size of a goose-quill.

12. Macaigne, in the "Societie Anatomique de Paris," 1891, reported a case of heart defect, there being a definite passage from the right ventricle to the aorta through the ventricular septum.

13. Dupré, in the same number, reported the case of a boy 4½ years of age; there was an opening 5 mm. in diameter between the right and left ventricles. This was situated below the insertion of the right aortic valve below the posterior coronary artery, in the median part of the upper membranous area.

14. Variot reported two cases in the "Journal Clinical et Therapeutique Infantiles," 1897. One was the heart of a boy aged 5½ months. There was communication between the left and right ventricles masked by the tricuspid valve and extending to within 0.5 cm. of the orifice of the pulmonary artery.

15. The second case was the heart of a girl aged 5½ years. Here there was a great loss of interventricular substance immedately below the origin of the aorta.

16. Emmanuel, in the "Reports of the Society for the Study of Disease in Children," 1906, reported the case of a boy whose heart showed a complete absence of the membraneous part of the interventricular septum, the aorta thus arising from both the left and right ventricles. The child was 7 years old.

17. Carpentier, in the same volume, cited the case of a female child of 2 years, whose heart showed a patent septum ventriculorum, the defect being one quarter inch in diameter.

REPORT OF CASE

Our specimen was obtained from the body of a man of 21 years, at an autopsy performed in the Cook County Hospital, Feb. 11, 1920, by Dr. H. Gideon Wells. The empty heart weighed 280 gm. The heart showed a dilated right ventricle which made up the entire apex. The left ventricle was contracted. The aortic and pulmonic valves were normal in appearance and competent to the water test. The wall of the left ventricle was 10 mm. thick, and the myocardium appeared normal. In the median and upper part of the interventricular septum, 11.5 mm. below the cusp of the right semilunar valve of the aorta, and directly below the origin of the right coronary artery, was an oval orifice measuring 7 mm. transversely and 5 mm. anteroposteriorly. Its margin was composed of a fold of raised endocardium protruding 0.25 mm. above the surrounding muscle surface. The loss of substance measured 1 mm., the thickness of the wall at this point.

On the right side, the opening was partially protected by adhesion of the tricuspid valve to the wall of the right ventricle, thus giving the opening a more nearly triangular shape on this side. The cusp partially occluding the opening was adherent about the posterior margin by several fibrous bands. In the cusp above the opening there were numerous fenestrations. Due to fusion there was practically a bicuspid valve, a large right cusp, free and functioning, and a small left cusp largely adherent to the interventricular septum. The small left cusp measured 2.2 cm. long and 1.5 cm. wide.

There were no other abnormalities found in the heart or other viscera except those appertaining to the pneumonia.

The patient had entered the hospital with a typical severe influenza pneumonia. At that time the apex beat was at the fifth interspace, 2 cm. to the left of the nipple line. The border of the heart showed an increase of 2 cm. to the left, otherwise the heart appeared to be normal on percussion. On auscultation there was a marked systolic murmur also a slight presystolic blow. The second pulmonic sound was accentuated.

He had been a laborer in a railroad freight house. He had been troubled with heart disease for years, having had dyspnea but never any edema. His mother said that follow-

ing a spree the dyspnea and so-called heart pains were much worse, but that the rest of the time there was little trouble. He was not a "blue" baby.

Dec. 13, 1920.

THE SACHS-GEORGI REACTION FOR SYPHILIS

A PRELIMINARY REPORT OF MORE THAN ONE THOUSAND COMPARATIVE WASSERMANN AND SACHS-GEORGI TESTS

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The Wassermann reaction for syphilis, despite its wide clinical acceptance, cannot be regarded as free from certain inherent defects. The mere fact that the test requires a considerable number of biologic reagents for its performance, all of which are to some degree variable and uncertain, is perhaps one of the reasons that the results of the test are not always reliable even when in the hands of the conscientious worker. We must furthermore recognize that a definite number of cases clinically positive are serologically negative. The standardization of the biologic reagents might seem a logical improvement, and efforts are being made in this direction by the German authorities. Efforts to simplify the technic have repeatedly been made, particularly since the recognition that the reaction is essentially physicochemical, not depending on specific immunologic alterations in the serum of the syphilitic. Perhaps the flocculation reactions, such as those described by Porges and Meyer, Herman-Perutz, Bruck, Klausner and others, gave evidence of progress in this direction, although none of them offered a real substitute for the Wassermann test.

The increased use of tests for syphilis, as well as the general shortage of the necessary biologic reagents incident to the war, made a reinvestigation of the problem desirable. Two tests have been developed: that of

Meinicke [1] and that of Sachs-Georgi,[2] which are evidently of considerable usefulness. Of these, the Sachs-Georgi, because of its remarkable simplicity as well as its seeming specificity, has found most favor. The obvious importance of simplified serologic procedure would warrant a careful comparison of such tests with the Wassermann reaction, and we have therefore examined over one thousand serums and spinal fluids by the Sachs-Georgi technic.

The technic of the Sachs-Georgi test which we have employed is the modification proposed by Mandelbaum,[3] which differs from the original in the use of smaller amounts of serum and antigen. The serum or spinal fluid to be tested must be absolutely clear after being centrifuged, free from cotton fibers or other particles. It is inactivated in the water bath at 56 C. for one-half hour. Three drops of serum are then mixed with 1 c.c. of sterile salt solution (0.85 per cent.). To this diluted serum, 0.5 c.c. of cholesterinized alcoholic beef heart antigen, which has been previously diluted 1 to 6 with 0.85 per cent. salt solution, is added. The tubes are then gently agitated and placed in the incubator at 37 C. for from eighteen to twenty-four hours. A reading is taken at this time; most of the positive serums will have flocculated. The tubes are kept at room temperature for the next twenty-four hours, and final readings are then made.

Apparatus.—Glassware must be perfectly clean. We have our tubes washed in tap water, then placed in an acid cleaning bath for several hours, washed in tap water and finally rinsed several times in distilled water. They are then dried in the hot air oven. Sterile pipets are used.

Serum.—The question that has been raised in the Wassermann technic concerning the use of active or inactive serum is also involved in the Sachs-Georgi test. Mandelbaum dilutes the fresh serum and then inactivates it before adding the antigen. We have used the inactivated serum, then diluted and added the antigen. Other observers prefer to keep the serum on ice several hours before inactivating, assuming that because of certain alterations brought about by the chilling of the seroglobulins, the reaction is made more sensitive.

Diluting Agents.—In the Wassermann reaction, approximate isotonicity seems sufficient, minor variations in the concentration of the salt being without effect on the reaction. In

1. Meinicke, E.: Berl. klin. Wchnschr., 1918, 4: 83.
2. Sachs, H., and Georgi, W.: Med. Klin., 14: 610, 1918.
3. Mandelbaum, M.: München. med. Wchnschr. 65: 294, 1918.

the Sachs-Georgi reaction we have found that reliable results can be obtained only when the salt solution is made up to 0.85 per cent. The salt solution should, of course, be sterilized.

Antigens.—The preparation of the proper antigen is perhaps the fundamental factor in the success or failure of the Sachs-Georgi reaction. Extracts from human, beef, pig, guinea-pig and sheep heart have been used, as well as from beef and syphilitic fetal liver. Our most satisfactory results have been obtained with an antigen thus prepared: 5 c.c. of alcohol (95 per cent.) per gram of moist heart substance was then poured over the mass and incubated at 37 C. for from eight to ten days. During this time the flask was shaken each day. The alcoholic extract was then filtered and cholesterinized. The amount of cholesterin needed varies with each antigen. We have found it good practice to titrate the antigen against positive and negative serums after adding various dilutions of cholesterin to small fractions of the antigen and selecting the proper amount of cholesterin to be added according to our actual serum titration. Sachs and Georgi thus prepared their antigen: To 100 c.c. of filtered beef heart extract and 200 c.c. of alcohol is added 13.5 c.c. of a 1 per cent. alcoholic solution of cholesterin.

Before use the antigen is diluted 1:6 with salt solution. The dilution must be made neither too slowly nor too rapidly. The extract when properly made is quite clear, the diluted antigen faintly opalescent and does not flocculate after standing several days. The antigen when diluted 1:10 serves very well as an antigen for the Wassermann reaction.

Incubation.—In the original Sachs-Georgi technic, the tubes were incubated for two hours and then placed at room temperature for twenty-four hours. Mandelbaum, Hauck,[4] Ammenshauser[5] and others have shown that better results are obtained if the incubation is prolonged for from eighteen to twenty-four hours. The tubes are then read and kept at room temperature for another twenty-four hours before the final reading is made. Sachs and Georgi have adopted this modification.

Reading of Results.—Most of the German workers have used the agglutinoscope devised by Kohn and Voit to read the results. A good magnifying lens from a dissecting microscope or even the ocular from a microscope can, however, be used with very satisfactory results if the tubes are held against a dark background. The flocculation may be very fine—smoky, finely granular—driven snow, or may finally be

4. Hauck, L.: Influence of Temperature on Sachs-Georgi Reaction, München. med. Wchnschr. 67: 369 (March 26) 1920.
5. Ammenshauser: Centralbl. f. Bakteriol. 84: 521, 1920. Originale.

precipitated at the bottom of the tube as a coarsely granular floccular mass. Gentle rotation or agitation of the tube aids observation. Negative cases remain perfectly clear for twenty-four hours, later a slight precipitate may collect at the bottom of the tube, but this can readily be differentiated from positive finding. In a general way, one can grade the degree of the reaction on a one to four plus basis; in a few cases we have recorded plus-minus readings. With the use of the agglutinoscope, the number of doubtful readings would probably be increased. We have found it useful to centrifuge doubtful tubes at low speed for half an hour and then pour off some of the supernatant fluid. By comparison with negative tubes similarly treated, minor differences become more apparent. We have also kept the tubes on ice after incubation, but have found no superiority over simple room temperature from this procedure.

RESULTS OF EXAMINATION

In Table 1 are recorded the results of 1,042 examinations made with the Wassermann and the Sachs-Georgi tests. The serums and cerebrospinal fluids were obtained from the serologists of the Cook County Hospital and the city board of health; their Wassermann reports were based on tests with from two to four antigens.

TABLE 1.—RESULTS WITH WASSERMANN AND SACHS-GEORGI TESTS

Reaction	Result								
	Positive			Negative			Anticomplementary		
Wassermann.....	+	±	0	+	±	0	+	±	0
Sachs-Georgi.....	163	5	3	44	9	634	2	0	3
Total.....	866								

In Table 1 it will be observed that in 163 cases there was an agreement of positive cases (18.8 per cent.) and in 634 an agreement of negative cases (73.2 per cent.), i. e., an agreement of 92 per cent.

The results with cerebrospinal fluid are given in Table 2.

TABLE 2.—RESULTS WITH CEREBROSPINAL FLUID

Reaction	Result								
	Positive			Negative			Anticomplementary		
Wassermann.....	+	±	0	+	±	0	+	±	0
Sachs-Georgi.....	36	6	3	7	2	121	1	0	0
Total.....	176								

The total agreement in this series was 157, or 89.2 per cent. Of the total number of serums and cerebrospinal fluids examined (1.042), sixty-two were found to give a positive or plus-minus Sachs-Georgi reaction while the Wassermann was negative. The details in our possession concerning these cases are recorded in Table 3.

TABLE 3.—CLINICAL CORRELATION OF CASES WITH POSITIVE SACHS-GEORGI REACTION AND NEGATIVE WASSERMANN REACTION

Number of Patient	Clinical Diagnosis on Admission	Clinical History	Treatment
xi-16	Suspected syphilis	Gonorrhea twice; chancre 2 mos. ago; now in second stage	None
ix-2	Chancroid	Primary syphilis; inguinal and epitrochlear glands; enlarged ulcer of scrotum	None
ix-32-34	Cerebral hemorrhage	History of chancre; rigid, irregular pupils; spinal fluid examination; pressure ++, globulins ++, 88 lymphocytes	None
ix-22	Cerebral hemorrhage	Paresis, left leg; patellar reflexes +++; absent abdominal and cremasteric reflexes	Potassium iodid and mercury
viii-12	Acute arthritis	History of transient attacks of paraplegia; roentgen ray, hypertrophic osteoarthritis; denies syphilitic infection	Improved under potossium iodid
viii-26	Chronic nephritis and endocarditis	Gonorrhea once, denies syphilis; pupils sluggish to light; absent patellar and cremasteric reflexes; shuffling gait; wife one miscarriage	None
vii-37	Broncho-pneumonia and syphilis	Gonorrhea and buboes; punched-out scar on prepuce; slight adenopathy; epitrochlear glands	Intravenous medication 11/9/20 N. W. U. Post-Grad. Med. Sch.
vii-64	General paresis	History of chancre and secondary syphilis; gastric crisis; tabetic gait and urinary incontinence; loss of memory	None
vi-8	General paresis	Chancre fourteen years ago; syphilitic erosion of nose; incontinence of urine; difficulty in walking at night; gastric crisis; patellar reflex, ++; Romberg sign, ++; Argyll Robertson pupils and scanning speech	Now on syphilitic treatment
vi-11-52	Syphilitic thrombosis	Chancre fifteen years ago; hemiplegia; amnesia; pupils sluggish; eyelids drooping; spinal fluid examination; pressure ++, globulin +, 16 cells	Has had six injections of arsphenamin
vi-24	Syphilitic epiphysitis	Congenital syphilis; palmar and plantar desquamation; rhagades about mouth; suggestive of syphilitic nose	None
vi-51	Crossed paralysis of sixth and seventh cranial nerves	Chancre two years ago; paralysis, right side of face; secondaries, hands and face; spastic and ataxic gait; Romberg, +++; patellar, +++; spinal fluid examination; pressure ++, globulins ++; 12 cells	None

TABLE 3.—Continued

Number of Patient	Clinical Diagnosis on Admission	Clinical History	Treatment
v-11	Syphilitic genital ulceration	Pregnant twenty times in twenty years: sixteen miscarriages, usually at two or three months	None
v-12	Chronic alcoholism, suspected tuberculosis	Chancre thirty-two years ago; rash twenty years ago; scars on penis, back and head	None
iii-1	Myocarditis; cardiac asthma	Chancre ten years ago; aneurism arch aorta	Arsphenamin 6 times, potassium iodid and mercury
iii-8	Syphilitic OHD general paresis	Perforated nasal septum; aortic regurgitation; tertiary syphilis; paresis, left side of face; cataract and posterior synechiae; aneurysmal dilatation of aorta	Syphilitic treatment, potassium iodid and mercury
iii-9	Cancer of stomach	Chancre four years ago; patellar reflex weak; gastric crisis	None
xii-58	Malaria	Chancre one year ago.....	None
xii-32	Hydrocele (syphilitic)	Chancre four years ago; secondary syphilis three years ago	None
xiii-23-50	Cerebrospinal syphilis	Chancre twenty-five years ago; loss of memory; scar on penis; drooping eyelids	None
xii-49	Chancre	Chancre three weeks ago.....	None
xiii-15	Acute epididymitis	Chancre three years ago; chronic gonorrheal urethritis; prostatic seminal vesiculitis and epididymitis	None
xiv-75	Cerebral syphilis	Chancre twenty-five years ago; Argyll Robertson pupils; spinal fluid examination; globulins ++; 80 cells	None
xiv-9	Traumatic epilepsy	Chancre twenty-four years ago; scar on penis and body	None

Cases in Which There Was No Complete Record Available from Hospital Sources, Most of the Serums Being Obtained from the Outpatient Department

xii-49	.....	History of chancre.....	None
xiii-15	Syphilis	History of chancre.....	None
i-55	Tertiary syphilis	.....	None
ix-15	Fractured mandible	History of chancre.....	None
xii-4P	Syphilis	History of chancre.....	One injection
i-46	Tabes	.....	None
v-11	Syphilitic ulcer of leg	.....	None
xiv-2	Pulmonary tuberculosis and syphilis	History of chancre.....	None
i-6	.....	Chancre on lip.....	None
i-9	.....	History of chancre 15 years ago...	None
i-13	Syphilis	.....	None
xiii-62P	Syphilis	Syphilis.....	Treated case

TABLE 3.—CONTINUED

Twenty Cases in Which the Wassermann Reaction Was Negative but the Sachs-Georgi Positive Without Any Evidence of Syphilis on the Part of the Patient, Either in the History or Clinical Finding

No. of Patient	Diagnosis or Symptoms	No. of Patient	Diagnosis or Symptoms
iv-10	Pain in legs; optic neuritis	xiii-4	Bronchitis; asthma
vii-69	Dementia praecox	xiii-1	Typhoid
vii-68	Chronic alcoholism	xiv-30	Chronic nephritis
viii-22	Routine; no diagnosis	xiv-33	Bilateral salpingitis
viii-15	Ovarian cyst	xiv-54	Chronic bronchitis
ix-28	Routine; no diagnosis	xiv-55	Suspected carcinoma of colon
xii-31	Routine; no diagnosis	xiv-29	Routine; no diagnosis
xiii-24	Lobar pneumonia	xiv-13	Cerebral hemorrhage
xiii-14	Acute cystitis	xiv-8	Constipation
xiii-10	Acute gonorrhea; lobar pnenumonia	xvii	Chronic arthritis and myocarditis

In six serums obtained from the serologist of the City Health Department, we obtained a positive Sachs-Georgi reaction with a negative Wassermann. These serums are sent in without diagnosis and we have no information concerning them.

It will be observed that the clinical history or the physical findings in thirty-six of these patients made a diagnosis of syphilis probable (58 per cent.). In twenty, the reaction seems nonspecific (32 per cent.), while in six cases we have no information that would assist in the determination of the correctness of the serologic finding.

From a summary of 17,186 serum tests reported by a number of observers and collected by Baumgärtel[6] (to which are added the 7,000 reported by him), Table 4 has been constructed.

TABLE 4.—RESULTS OF SERUM TESTS

Reaction	Result								
Wassermann	Positive			Negative			Doubtful		
Sachs-Georgi	+	±	0	+	±	0	+	±	0
	5,808	282	514	686	221	15,950	154	246	325
Total	24,186								

It will be observed that in 5,808 positive cases and in 15,950 negative cases, there was complete agreement, as well as in 246 doubtful reactions, 91 per cent. of the total. Of the discrepancies (9 per cent.) the cases in which the Wassermann reaction was positive and the Sachs-Georgi negative or doubtful, numbered 1,121, or 51 per cent.; those in which the Wassermann was negative while the Sachs-Georgi was positive or doubtful numbered 1,061, or 48 per cent. These collected results represent the observations made with various modifications of technic, particularly in regard to incubation time. The cases in which the Wassermann reaction was nega-

6. Baumgärtel, T.: Parallel Wassermann and Sachs-Georgi Tests, München. med. Wchnschr. 67: 421 (April 9) 1920.

tive while the Sachs-Georgi was positive include a considerable number of treated cases of primary and parasyphilitic disease, as well as a small group of diseases of nonsyphilitic basis. The latter may possibly be eliminated with further study of the preparation of the antigen. Just as the Wassermann reaction becomes nonspecific to a considerable degree when the antigen is fortified with too much cholesterol, so perhaps the acuity of the Sachs-Georgi reaction can be modified when once we become familiar with its range.

DISCUSSION

An examination of the results tabulated herewith makes it evident that this flocculation test very closely approximates the results obtained with the classical Wassermann reaction and may in some ways prove superior to it. While for the time being we must accept the Wassermann test as our standard of comparison, we should by no means lose sight of the fact that this standard is not infallible. While the error does not lie in the direction of nonspecificity, a definite number of positive syphilitic cases do not react with the Wassermann technic and are either classed as negative or yield doubtful readings. It seems that this relatively large group of cases flocculate quite readily with the Sachs-Georgi method, as will be apparent from a perusal of some of the histories and clinical findings recorded in Table 2. Only in thirty-two cases of the series were the Sachs-Georgi reactions positive in the absence of positive clinical findings or history.

We can enter here but briefly into a discussion of the mechanism that seems to underlie the flocculation made grossly apparent in the Sachs-Georgi reaction, and which is closely related to the ultramicroscopic colloidal alterations that have been described as taking place in the Wassermann reaction when the antigen is added to the serum. Both the globulins and the lipoids of the syphilitic serum seem altered to some degree, and Schmidt,[7] Hirschfeld and Klinger,[8] Sachs,[9] and Meinicke[10] are of the opinion that the alteration involves a peculiar lipotropic property of the serum globulins, the lipoglobulin aggregate being easily precipitated in solutions that are iso-electric for the globulins. Neukirch[11] places the hydrogen-ion concentration represented in a 0.85 per cent. salt solution as the optimum for the precipitation of the globulins, i. e., the identical concentration found most satisfactory for use in the Sachs-Georgi technic. From the point

7. Schmidt: Ztschr. f. Hyg. u. Infectionskrankh. 69: 513, 1911.
8. Hirschfeld and Klinger: Ztschr. f. Immunitatsforsch. 21: 40, 1914.
9. Sachs, H.: Kolloid-Ztschr. 24: 123, 1919.
10. Meinicke, E.: München. med. Wchnschr. 66: 932, 1919.
11. Neukirch, P.: Ztschr. f. Immunitatsforsch. u. exper. Therap. 29: 498, 1920.

of view of its theoretical interest, we wish to call attention to the two phase reaction of Meinicke for syphilis. This reaction involves the precipitation of the globulins of the serum in both negative and positive serums by simple dilution after the addition of antigen; then the addition of varying dilutions of salt solution to the serums so altered. In positive cases, the lipoglobulin precipitate remains unchanged; in negative cases the precipitates redissolve.

The Sachs-Georgi reaction is exceptionally simple, and once a suitable antigen has been prepared, it can be carried out with ease. The use of the complement-amboceptor-hemolytic system used in the Wassermann reaction is after all a cumbersome method of making apparent the colloidal alterations which are at the basis of these reactions for syphilis. Ultimately such a system must be replaced by a reaction simpler in character, requiring fewer reagents and less manipulation. Whether such a reaction will be of the flocculation type, such as the Sachs-Georgi, or will be purely chemical, is for the present not in the range of discussion. It is evident, however, that the Sachs-Georgi, reaction, even in its present form, offers a valuable contribution because of its simplicity and its apparent practicability. The fact, too, that it is frequently positive in those syphilitic cases which do not give a positive Wassermann reaction, makes it of value as an additional test to be used in conjunction with the Wassermann technic. The fact that a relatively small percentage of nonspecific reactions is obtained should not detract from its ultimate usefulness; the earlier work with the Wassermann reaction was handicapped until the preparation of antigens was better understood.

CONCLUSIONS

An examination of 1,042 sera and cerebrospinal fluids by means of the Wassermann and the Sachs-Georgi reactions demonstrated a close parallelism of the two reactions (92 per cent.).

In sixty-two cases in which the Wassermann reaction was negative while the Sachs-Georgi reaction was positive or doubtful, the clinical history or examination revealed evidence of syphilis in 58 per cent.

The technic of the Sachs-Georgi reaction is simple; only one biologic reagent is required (antigen) instead of the four used in the Wassermann test (antigen, amboceptor, complement and red blood cells). This

simplicity adds to the uniformity of the results. The ultimate specificity depends on the preparation of a proper antigen.

Because of its simplicity, and the fact that it is frequently positive in syphilitic cases when the Wassermann test is negative, we are of the opinion that the Sachs-Georgi reaction offers a valuable aid in the routine examination for syphilis when used in conjunction with the Wassermann reaction.

Dec. 13, 1920.

LEUKOCYTOSIS AND BLOOD ALKALI RESERVE CHANGES (VAN SLYKE) WITH EXPERIMENTAL INFECTIONS

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The alkali reserve (Van Slyke) of the whole blood of rabbits was determined at short intervals after intravenous injection of the following bacteria: *Bacillus typhosus, Bacillus dysenteriae* (Flexner), *Bacillus coli, Streptococcus hemolyticus* (pyogenes), *Streptococcus viridans* (mitis), *Bacillus diphtheriae, Bacillus pneumoniae,* and *Bacillus aerogenes capsulatus.* At the time of each determination, the number of leukocytes in the blood was also determined. Within 2 to 4 hours after the injection of the bacteria, there is a marked leukopenia and a diminution of the alkali reserve of the blood. During the next 12 to 18 hours, when the infection is rapidly overcome, there is a rapid increase in the number of leukocytes, and a return to normal or slightly above of the alkali reserve. The alkali reserve and the number of leukocytes then return promptly to normal.

This reaction is modified in animals where the infection is not overcome promptly in 48 to 72 hours. In them the alkali reserve remains low following the initial diminution while the leukocytes increase in number. With the continued high leukocytosis the alkali reserve remains depressed, but with the latter becoming

normal, the leukocytes decrease and the curves plotting these reactions tend to become parallel. The return to normal of the alkali reserve after a marked and prolonged depression is followed frequently by a short period of increased alkali reserve (alkalosis). There is little change in the number of leukocytes of the blood after injections of bacteria not followed by a lowered alkali reserve.

In the experiments mentioned, a marked leukocytosis is regularly preceded by a marked and prolonged depression of the alkali reserve of the blood.

It is suggested that the factors associated with the depression of the alkali reserve or the depression of the alkali reserve itself may furnish the stimulus for the subsequent generalized leukocytosis.

Dec. 13, 1920.

RIGOR MORTIS IN SMOOTH MUSCLE

From the Pathological Laboratory of St. Luke's Hospital, Chicago.

EDWIN F. HIRSCH

Rigor mortis has been studied largely in skeletal muscle, and such conclusions regarding its occurrence in smooth muscle seem to have been made by inference rather than by actual experimental observations. In fact, according to certain statements in the literature, there is some doubt as to the actual occurrence of rigor mortis in smooth muscle. Fibromyomas and uteri contain a large amount of smooth muscle tissue. Pieces of these mounted in a suitable apparatus immediately after removal contract to a maximum, at first rapidly, then more slowly, usually within 30 minutes. Forceful extension of the muscle tissue is followed by a similar contraction, but after about one hour contractility disappears, and no contraction occurs after forceful extension.

Ten gram pieces of tissue placed in 15 c.c. of "conductivity" water for 15 minutes regularly give an acid reaction (colorimetric H-ion method) to the liquid, excepting those from fibromyomas that are in "red

degeneration." Some of these fluids respond to the ferric chloride test for lactic acid. The maximum acidity determined colorimetrically is expressed by a H-ion concentration of p_H 6.0. Tissues of fibromyomas in red degeneration do not become rigid nor do they become distinctly acid.

The alkali reserve of fibromyoma tissue fluid diminishes rapidly during the first 1 to 1½ hours after removal. A similar and parallel diminution of the reducing sugar content of fibromyoma tissue fluid occurs. This sugar does not disappear completely.

SUMMARY

There is a postoperative (postmortem) rigor of smooth muscle which is manifested by changes known in skeletal muscle as rigor mortis. Each variety of muscle in this change contracts, and is accompanied by a distinct tissue acidity. With smooth muscle this acidity develops and increases rapidly to a maximum, is paralleled closely by a rapid diminution of its reducing carbohydrates, and by a decrease of its alkali reserve. There is a fairly uniform maximum tissue acidity (p_H 6.0) in the rigor mortis of fibromyomas, part of which at least is due to lactic acid.

Jan. 10, 1921.

THE STREPTOCOCCI AND PNEUMOCOCCI OF THE ADENOIDS

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Many dangerous bacteria have been cultured from the nasopharynx and it has been assumed that these organisms flourish in large numbers about the adenoid vegetations. In order to determine more accurately the nature of the bacterial flora in this region and to ascertain the extent to which the adenoids like the faucial tonsils harbor these micro-organisms, a bacteriologic

study of the adenoids was undertaken. The present report concerns itself only with the streptococci and the pneumococci.

The adenoids were removed at the Cook County hospital during the months of April, May and June, 1920 from children varying from 5 to 16 years of age. The La Force adenotome was employed. Macerated adenoid tissue was discarded. In most instances the adenoids consisted of hyperplastic lymphoid tissue from 1 to 1.5 cm. square and 0.5 to 1 cm. thick. Fatty débris and cholesterol crystals in a few instances were formed in the tissues. Real pus was not encountered. Structurally in most cases the adenoids presented three to six folds, in others fibrous union had taken place between the folds leaving pits not unlike the crypts of the tonsils, although not as deep. Most of specimens revealed both the folds and the crypt-like depressions.

Altogether adenoids from 103 individuals were examined. In 21 instances the tonsils were collected from the same patients and swabs made from the nasopharynx by means of the West tube before adenoidectomy. The adenoids and tonsils were collected separately in sterile gauze and cultures made in 1 to 4 hours after removal. Cultures were made from the surface of the adenoids, and with a loop after separating the folds with sterile forceps, cultures were obtained from the depths of the folds and the crypt-like depressions. The tonsils were incised transversely with a sterile knife and material for culture obtained from the bottom of the crypts.

Cultures were made by streaking the surface of blood-agar plates and also by inoculating melted infusion-agar titrated to p_H 7.6 to which defibrinated human blood was added in proportion of 1 part of blood to 10 or 12 parts of agar, and pouring into Petri dishes. The plates were incubated at 37.5 C. and examined at the end of 24 and 48 hours. Both the streak and pour plates were studied for hemolytic and green-forming colonies.

Colonies of streptococci, small, discrete, biconvex, forming zones of complete hemolysis 1 to 4 mm. across, corresponding to the Beta type of the *Streptococcus*

hemolyticus, were present in 58 per cent. of the nasopharynx swabs and in the cultures of the surface of the extirpated adenoids. They were seldom predominant and numerous in only nine instances. From the cultures made from the depths of the folds and depressions they were obtained in 61 per cent. in larger numbers, being obtained in pure culture in 3 instances and in large numbers in 18. The above figures were obtained from the examination of the poured plates. It is interesting to note that from the streak plates the hemolytic streptococci were observed in only 26 per cent. of the cultures of the adenoid surface and in 37 per cent. from the depths, demonstrating definitely the superiority of the poured plate in the detection and isolation of the *Streptococcus hemolyticus.*

Of the 21 pairs of tonsils 20, or 95 per cent. revealed hemolytic streptococci. In the adenoids of the same individuals these organisms occurred in 15 instances, giving 5 instances in which the streptococci were recovered from the crypts of the tonsils and not from the adenoids. Furthermore, the tonsillar crypts harbor these bacteria in greater numbers as compared with the adenoid. However, the crypt-like structures of the adenoids, like the crypts of the tonsils, frequently revealed the streptococci in large numbers, demonstrating the tendency of the hemolytic streptococcus to flourish in the deep depressions of the lymphoid tissues of the oropharynx and nasopharynx.

Sixty-five strains, of which 60 were found in the adenoids, were isolated and studied. All were bile insoluble and hemolytic in the subcultures. All fermented lactose, all but 3, salicin, 3 fermented mannite, and 2 inulin. Inulin from another source was not fermented by the two strains. According to Holman's classification, 59 were *Streptococcus pyogenes,* 2 *Streptococcus infrequens,* 2 *Streptococcus anginosus* and 1 *Streptococcus hemolyticus* III. Litmus milk was acidified by all in 7 to 10 days, 10 coagulating spontaneously and the remainder coagulated on gentle heating. Two c.c. of a 48-hour serum broth culture or one washed blood agar

slant given intravenously to young rabbits produced arthritis and endocarditis, often resulting fatally in 1 to 10 days.

The narrow indefinitely hemolytic colonies corresponding to the Alpha type of Smith and Brown were encountered in 20 per cent. and were included in the non-hemolytic or *Streptococcus viridans* group.

Green producing organisms of three types were isolated and studied. The *Streptococcus viridans* type occurred as small, round, gray, discrete biconvex colonies surrounded by a grayish-green zone. The pneumococcus usually presented flatter, often checker-like, colonies surrounded by a similar often darker green zone of methemoglobin. Lastly, there were somewhat larger green moist colonies often mucoid, showing marked tendency to become confluent, corresponding to the pneumococcus mucosus type and to the so-called Mathers type of streptococcus.

Bile solubility and inulin fermentation was carried out upon the various strains. The bile insoluble, non-inulin fermenting strains corresponding to the *Streptococcus viridans* occurred in 89 per cent. The bile soluble, inulin fermenting strains corresponding to the pneumococcus group were found in 65 per cent. In four instances the pneumococcus occurred in practically pure culture. In the 21 pairs of tonsils the pneumococcus and *Streptococcus viridans* were found with the same frequency and in about the same numbers as in the adenoids.

Forty viridan strains were studied by means of litmus milk and sugar fermentation. All acidified and usually coagulated milk in 7 to 10 days. Lactose were fermented by all, salicin by 14, mannite by 3. According to Holman's classification, about 6 per cent. were *Streptococcus fecalis*, 30 per cent. *Streptococcus mitis* and the remainder *Streptococcus salivarius*.

Small colorless colonies resembling the streptococcus but causing neither hemolysis nor methemoglobin formation were noted in 12 per cent. These have been referred to as indifferent streptococci.

The moist green-forming colonies were somewhat variable in their appearance. Altogether they were encountered in 26 instances. Of these 9 were distinctly mucoid, convex like the *Pneumococcus mucosus*. The other 17, although quite moist, showed a tendency to flattening and conform to the descriptions of the Mathers' type. Of the former 9 strains 6 were bile soluble and 3 insoluble. Three of these strains therefore conform to the *Streptococcus mucosus* type. Of the 17 Mathers strains 9 were bile soluble, 8 insoluble, 6 fermented inulin and 11 did not. Morphologically all the above strains revealed capsulated diplococci often lanceolate shaped. The Mathers' type often revealed a tendency to the formation of chains of cocci.

Agglutination with Type I, II, and III sera was conducted upon the bile soluble organisms. Eighty-five per cent of the 65 strains of pneumococci were Type IV, 13 per cent, Type III, and 2 per cent. Type II. Two strains agglutinated by Type III serum were not mucoid. Two strains of Mathers' type were agglutinated by Type III serum.

CONCLUSIONS

Hemolytic streptococci occurred in 61 per cent. of adenoids from 103 children. *Streptococcus viridans* were found in 89 per cent., indifferent streptococci in 12 per cent., and the *Streptococcus mocosus* in 3 per cent. The Mathers streptococcus occurred in 17 per cent.

Pneumococci were present in 65 per cent., 2 per cent. of which were Type II, 13 per cent. Type III, and 85 per cent. Type IV.

Jan. 10, 1921.

CULTURAL AND SEROLOGIC OBSERVATIONS OF GONOCOCCUS INFECTION IN THE MALE*

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The necessary considerations for securing positive cultures in latent gonorrheal infections are described under: (1) Conditions favorable for growth of gonococci; (2) suitable medium; (3) collection of suspected material, and (4) methods of identification of the gonococcus.

A series of one hundred selected cases were studied. The complement fixation test was made on the serum of each patient. A description of the antigen and the technic of the test is given.

Gonorrheal precipitin tests were also made on 90 per cent. of the serums. A series of provocative tests were made by the use of local and general reactions. The clinical observations were analyzed and correlated with the laboratory tests.

It is concluded that: (1) cultures of prostate and seminal fluids and first urine sediment, carefully collected, are the most reliable single means of determining whether or not a gonorrhea is cured. For this purpose phosphate agar with blood and ascites fluid is suitable and the inoculated plates should be incubated under reduced oxygen tension; (2) the complement fixation test is a valuable aid, but the results should be taken in conjunction with the cultural results. Low degree positive fixation may persist up to a year after positive smears and cultures can be obtained. However, with positive serologic reaction, cultures should be repeated at intervals and the patient kept under observation until the serologic tests give negative results; (3) the gonococcus may be identified by agglutination tests with polyvalent antigonococcus serum; (4) a satisfactory antigen can be easily prepared as described; (5) the

* The complete paper is printed in Jour. Am. Med. Assn., 1921, **76**: p. 225.

precipitin test appears less sensitive, but because of its greater simplicity it may be used as a substitute for complement fixation under special circumstances; (6) the use of provocation tests before taking cultures and smears is of no advantage, and (7) the pus cell content of smears and macroscopic urinary appearances may be misleading, and by themselves constitute no safe index of cure.

Jan. 10, 1921.

THE INFLUENZA BACILLI OF THE ADENOIDS AND TONSILS

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To determine more accurately the incidence of the Pfeiffer bacillus a bacteriologic examination of the excised adenoids and tonsils for this organism was undertaken. The adenoids and tonsils were obtained at the Cook County hospital from children from 5 to 16 years of age who were without fever or acute inflammations of the respiratory tract. In 25 nasopharygeal swabs were obtained before adenoidectomy. Cultures were made from the depths between the folds and from the bottoms of the slits or crypt-like depressions of the adenoids and from the bottoms of the crypts of the extirpated tonsils. Inoculations were made upon fresh blood agar plated and upon blood agar which had been previously heated to 90 degrees C. until the media assumed a chocolate color.

RESULTS

Upon the chocolate plates the influenza bacilli occurred in the culture of the adenoids of 115 individuals in 47, or 40.9 per cent., and from the tonsils of the same persons in 62, or 53.9 per cent. In the nasopharyngeal swabs they were found in 10, or 40 per cent. In each instance in which the organism was found in the adenoids it was also recovered from the tonsils. From the depths of the adenoid folds the

bacilli were encountered once where they did not grow in the culture of the nasopharyngeal swab. It was noted that these bacteria were more numerous in the adenoids than the swabs. Upon the fresh blood agar plated the bacilli grew as small translucent dewdrop colonies, occasionally showing strikingly the tendency to grow in clusters immediately around the other colonies.

The bacilli appeared as small gram negative rods often plemorphic, revealing coccoid and thread-like forms, particularly on the subcultures. They failed to grow on infusion agar and exhibited the characteristic property of symbiosis when grown with another organism.

CONCLUSIONS

Gram negative pleomorphic, hemoglobinophilic bacilli, revealing the characteristic property of symbiosis, were isolated in 40.9 per cent. of the excised adenoids and 53.9 per cent of the excised tonsils of 115 invididuals. In the nasopharynx they were present in 40 per cent of 25 individuals and in fewer numbers.

The tonsils and adenoids, therefore, are foci where influenza bacilli (Pfeiffer) commonly flourish.

Feb. 14, 1921.

THE FLORA OF THE NASOPHARYNX IN TONSILLECTOMIZED AND NON-TONSILLECTOMIZED CHILDREN

WITH SPECIAL REFERENCE TO THE PNEUMOCOCCUS, STREPTOCOCCUS HEMOLYTICUS AND B. INFLUENZAE (PFEIFFER)

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AND
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A bacteriologic study of the nasopharynx was undertaken to determine the change in the flora of this region following the removal of the adenoids and tonsils. A

group of healthy children of the Marks Nathan Orphan Home was selected, some of whom had had their tonsils and adenoids removed from 2 months to 5 years previously. These individuals were without fever or acute inflammations of the respiratory passages. The cultures were obtained by means of a curved wire swab with which inoculations of blood agar and heated blood agar plates and infusion broth were immediately made. The infusion broth after 24 hours' incubation was subsequently inoculated into blood agar and poured plates made. The cultures were examined for the pneumococcus, *Streptococcus hemolyticus* and *B. influenzae*.

RESULTS

Pneumococcus.—Green forming colonies were subcultured and identified as pneumococci by morphology, inulin fermentation and bile solubility. Agglutination with specific Type I, II and III sera was carried upon the pure cultures. Of 49 children whose tonsils and adenoids were absent the pneumococcus was found in 15, or 32.5 per cent. Ten strains were Type IV, two Type III, one Type IIa, and two Type I. In one instance a green streptococcus bile insoluble but which fermented inulin was encountered. Of 68 children with adenoid and tonsils 21, or 32.3 per cent, harbored pneumococci, of which 20 were Type IV, and one Type IIa. In two instances a green streptococcus bile insoluble but fermenting inulin was noted. Eight children who had remnants of tonsils gave three positive cultures for pneumococci, of which two were Type IV and one Type III. It was found that the colonies on the plates from the tonsillectomized were fewer in number than from the nontonsillectomized.

Streptococcus Hemolyticus.—The Beta type of the hemolytic streptococcus occurred in 11 (40.8 per cent.) of 27 tonsillectomized and 24 (60 per cent.) of 40 nontonsillectomized children. In 8 children with remnants of tonsils these organisms were present in 3. Here also it was noted that the number of colonies of hemolytic streptococci were decidedly less numerous in the tonsillectomized than the nontonsillectomized.

B. Influenzae (*Pfeiffer*).—The observations were made from the heated blood plates. Eight (26.5 per cent.) of 29 tonsillectomized and 13 (37 per cent.) of 35 nontonsillectomized children gave positive results. Of 8 with remnants, 4 harbored the influenza bacillus. Fewer colonies were present on the plates from the tonsillectomized than from the other groups.

CONCLUSIONS

Normal children harbor pneumococci, hemolytic streptococci, and *B. influenzae* in their nasopharynx.

The incidence and numbers of these organisms is less in tonsillectomized than nontonsillectomized children.

Feb. 14, 1921.

TRANSACTIONS OF THE
CHICAGO PATHOLOGICAL SOCIETY

VOL. XI. JUNE 1, 1921. NO. 5

SOME LESIONS OF THE HYPOPHYSIS

J. P. SIMONDS

A satisfactory correlation of the pathologic changes in the hypophysis and the clinical manifestations, such as abnormalities of growth, alleged to be due to such changes still remains to be made. After an extensive survey of the literature of the morbid anatomy and histopathology of the hypophysis, and a study of something more than one hundred hypophyses obtained at routine postmortem examinations, it has seemed that the most effective method of solving this problem lies in a systematic study of all hypophyses removed at necropsies.

One reason for our lack of accurate knowledge of the pathology of the hypophysis lies, in part, in the neglect of this organ by pathologists themselves. Too frequently this gland is not examined even in those cases in which the head is opened. When it is remembered that the greater part of our knowledge of the relation of pathologic changes in the hypophysis to acromegaly, Froelich's syndrome and diabetes insipidus, is based upon results of postmortem examinations rather than upon experimental work, the claim that necropsies are the source, *par excellence*, of material for the solution of this question, would seem to be justified. The attempts at its solution by means of experiments upon animals have been failures. To be convinced of this, one only need consult the abstract department of any number of *Endocrinology* to find different experimenters obtaining diametrically opposite

results and arriving at absolutely incompatible conclusions from similar experimental processes.

In attempting to correlate pathologic changes in the hypophysis with clinical manifestations, certain very definite difficulties are encountered and must be duly considered. In the first place, the normal histology of the hypophysis has not been established in all of its details. The gross and microscopic division of the gland into anterior, middle and posterior lobes; and the recognition of three types of cells in the anterior lobe, namely, chromophobe, eosinophile and basophile cells; is about as far as histologic description has gone. No norm has been established for the relative proportion of these cells to each other. A study of a large number of apparently normal hypophyses reveals the reason for this in the great variations in the relative numbers of the different types of cells in such hypophyses.

In the second place, the histogenesis of the cells of the anterior lobe is still in dispute. Benda considered the three types of cells as varying stages in the secretory activity of one and the same type of cell. Scaffidi, on the other hand, believed the basophiles and eosinophiles to be separate and distinct forms. Kraus has introduced a more elaborate classification into chief (or chromophobe) cells, transition cells, eosinophiles, basophiles, and the cells of pregnancy.

In the third place, the factor of safety in the hypophysis is not known. This appears to be relatively high because a considerable number of cases are on record in which a large part of the gland had been destroyed without any of the accompanying abnormalities of growth or of fat deposits, or of other clinical manifestations usually assigned to hypofunction of one or more parts of the gland.

Photomicrographs of the following lesions were presented and discussed:

1. A small abscess in the posterior lobe, from a patient with multiple septic infacts in many organs of the body.

2. Growth of cells of the middle lobe backward into the neurohypophysis. This may occur in the form of

rather large solid masses, or as narrow finger-like processes. This condition is relatively common in old age.

3. Islands of abnormal cells in the posterior lobe. These cells are unlike any of the cells of the anterior or middle lobe, and are not connected, as shown by serial sections, with the backward growth of cells from the middle lobe, as shown in No. 2. The significance of these cells is not at present known.

4. Hemangioma-like structures in the anterior lobe. These appear to be quite constant and can be easily demonstrated in serial sections. The blood supply of the anterior lobe enters along the groove between the anterior and posterior lobes. These vessels pass to each lateral half of the anterior lobe, and, at about the center of each half, form the structure shown in the photomicrograph.

5. Round cell infiltration of the middle lobe. Small masses of lymphoid cells are occasionally found along the line of contact between the middle and posterior lobes. Their significance is not known.

6. Congenital syphilis of the hypophysis. The characteristic feature is a uniform increase of connective tissue between the cords of cells in the anterior lobe.

7. Adenoma of the hypophysis. The tumor measured slightly more than 1 mm. in diameter and was composed of chief or chromophobe cells. The specimen obtained was from the body of an aged colored man. There was no definite evidence of acromegaly.

Jan. 10, 1921

MALIGNANT TUMORS OF THE TESTIS

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As the result of an analysis of the previous literature and of the study of nineteen cases of his own, Ewing,[1] in 1911, was led to doubt the occurrence of homologous benign connective tissue tumors of the

1. Ewing, James: Teratoma testis and its derivatives, Surg., Gynec. & Obst., 1911, xii, 230.

testis and the derivation of malignant tumors from the normal, differentiated elements of this organ. He held that testicular tumors of other than teratomatous origin are extremely rare, and agreed with a number of previous writers that most of the so-called sarcomas of the testis are really epithelial tumors. He differed, however, from a number of competent students of the subject in that he derived the malignant epithelial tumors, as well as the benign mesoblastic ones, from teratomas. Without having given any particular study to the subject, the writer was inclined to accept Ewing's views, largely because of the simplification which they brought into a most complicated field. Ewing's important contribution has apparently remained unknown to many surgeons and pathologists, if one may draw such a conclusion from the number of reports of sarcoma of the testis which have appeared since his paper. The writer's experience leads him to believe that the surgeon considers every testicular tumor which is clinically malignant a sarcoma; the acceptance and use of Ewing's designation of embryonal carcinoma, instead of the expected sarcoma, has several times resulted in misunderstanding, as between surgeon and pathologist, in regard to such tumors. This finally made it necessary to review the subject upon the basis of such material as was available. The result of this study has made it impossible to accept Ewing's conception in its entirety, but still leaves us convinced of the infrequency of sarcoma.

If we leave out of consideration the clinical reports of sarcoma, because they have not as a rule been based upon any very careful histologic study of the individual tumors or have not indicated any very thorough knowledge of the subject, there are a number of careful studies upon the histogenesis of malignant tumors of the testis which have appeared since Ewing's [1] paper. While practically all of these agree, in accord with Ewing, that the large cell tumor, which appears to be the most frequent type, is an epithelial tumor and not a sarcoma, contrary to the usually accepted surgical view, very few agree with Ewing in deriving all the malignant tumors from teratomas.

Frank [2] held that the large cell tumor, the type concerning whose nature and origin there has been the greatest divergence of opinion, arises from the epithelium of the convoluted seminal tubules. Tumors of a more glandular character he believed to be derived from the straight tubules and also from mixed tumors; he accepted the occurrence of sarcoma derived from the interstitial cells. The large cell tumors which Stopatto [3] derived from the interstitial cells were almost certainly the same as the tumors which Frank, Chevassu, Birch-Hirschfeld and others believed to spring from germinal epithelium. Vecchi,[4] who studied a group of mixed tumors, concluded that most of these tumors are not teratomas but are mesoblastic mixed tumors derived from totipotent cells of the urogenital anlage; he believed that only three of the twenty-four mixed tumors studied by him were teratomatous, i.e., derived from misplaced blastomeres. Sakaguchi's [5] conclusions are in general agreement with those of Frank; the large cell tumors originate from spermatogonia, the glandular tumors from the straight tubules and not from teratomas. Geist and Thalheimer [6] postulate a triple origin for the malignant tumors, as compared with the dual origin accepted by Sakaguchi; the large cell tumors come from spermatogonia, the adenocarcinomatous ones from straight tubules; thus far they are in agreement with Sakaguchi, but they admit the further possibility of the origin of adenocarcinomas in teratomas. O'Crowley and Martland [7] appear to be the only writers who have unreservedly accepted Ewing's views.

The material upon which the present study is based has been collected in the pathologic laboratory of the Michael Reese Hospital in the course of the last twelve

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3. Stopatto, U.: Die Zwischenzellentumoren des Hodens, Zieglers Betitr. z. path. Anat., etc., 1911, 1, 113.

4. Vecchi, A.: Teratome, teratoide Geschwülste und Mischtumoren des Hodens, Deut. Ztschr. f. klin. Chir., 1912, cxiv, 104.

5. Sakaguchi, Y.: Zur Kentniss der malignen Hodentumoren, vor allem der epithelialen, Deut. Ztschr. f. klin. Chir., 1913, cxxv, 294.

6. Geist, S. H., and Thalmeimer, W.: Histopathology of carcinoma of the testicle, Ann. Surg., 1917, lxvi, 571.

7. O'Crowley, C. R., and Martland, H. S.: New-growths of the testis, Surg., Gynec. & Obst., 1919, xxviii, 486.

years and consists of fifteen malignant tumors of the testis. Even a superficial examination divides these tumors at once into two main groups: I, the soft, medullary, large cell tumors, so frequently described as sarcoma; II, tumors in which the atypical tissue has a more glandular or adenocarcinomatous character. The detailed histologic study of these tumors has been published elsewhere.[8]

Fig. 1. Large cell, medullary tumor of testis. Spermatocytoma. This tumor contains no heterologous structures. Photomicrograph, × 80.

Large Cell Tumors.—Six of our fifteen tumors belong to this group. Common to all of them is their soft, cellular, medullary character (Fig. 1), which has been responsible for the widespread use of the term "large round cell sarcoma" for neoplasms of this kind. An alveolar arrangement of the cells can usually be detected; in some examples it is quite distinct in places, while in others an alveolar character is more difficult

8. Schultz, O. T., and Eisendrath, D. N.: The histogenesis of malignant tumors of the testicle, Arch. Surg., 1921, ii, 493.

to determine. In none of the tumors is there any semblance of a glandular arrangement. In not one of the six tumors of this group is heterologous tissue present. Dense groups of lymphocytes occur frequently, but they do not have the appearance of true lymphoid tissue. Most characteristic is the type of the tumor cell. The latter is large. It is irregularly polyhedral in shape, due to the pressure which the cells exert upon each other. The cytoplasm stains faintly and is rather coarsely alveolar. The nucleus is absolutely and relatively large and has a distinct membrane and one or two small nucleoli. The chromatin, in different tumors and sometimes in the same tumor, shows differences in arrangement and distribution, but these differences all fall into a definite series. In some tumors distinct chromatin granules do not occur or are so fine that they can not be readily seen. In others, the chromatin is aggregated into distinct but still small granules, which are arrranged upon a finely meshed intranuclear network. In still other tumors the granules are still larger and fewer in number, as the result of further aggregation and condensation of chromatin upon the intranuclear network, which is now more coarsely meshed.

The nuclear morphology which has been described appears to be very characteristic of the group of tumors under consideration. Malignant tumors of definite teratomatous origin may be composed of large cells with relatively large vesicular nuclei, but such nuclei are quite distinctly different, in that they have the characteristics of young tissue nuclei. The nuclear type under consideration is not found in normal somatic nuclei, either young or old, but it is characteristic of the sex cells of the seminal tubules. Not only do the cells of this group of tumors bear the greatest resemblance to the cells of the spermatogenic cycle, but the converse is also true. The nuclei bear no resemblance to those of normal somatic cells or to those of tumors derived from somatic cells.

Adenocarcinomatous Tumors.—The atypical epithelial tissue of some of our tumors of this group occurs in the form of markedly glandular structures which

may be very suggestive of a carcinoma of intestinal origin (Fig. 2). In other tumors the cells of the alveoli are not of such an extreme columnar type; they are lower, vary in size and shape, and often completely fill the alveoli, so that the glandular character may be rather indistinct in some fields. Often they form papillary ingrowths into epithelial lined spaces (Fig. 3). In one tumor of this group the atypical tissue is not at all glandular in character, but forms

Fig. 2. Adenocarcinomatous tissue in a tumor which contains heterologous elements. Embryonal carcinoma of hypoblastic origin. Photomicrograph, × 80.

solid cellular masses, which can be traced directly to the well differentiated, low cuboidal epithelium of cystic spaces (Fig. 4). These alveoli bear a striking resemblance to the basal cell carcinoma of the epidermis. In many places in this tumor the cells do not form definite alveoli, but occur as poorly defined, cellular areas which look very much like sarcoma. In such areas the individual cells take on a spindle shape, which increases the similarity to sarcoma, but the

poorly defined areas and their spindle cells are directly continuous with the well defined carcinomatous alveoli composed of closely placed, irregularly polyhedral cells. The resemblance to sarcoma which this tumor has in many areas is also a characteristic of the epidermal basal cell carcinoma. Nine of our fifteen tumors belong to this second group.

Six of the nine tumors which make up the second group, contain definite heterologous tissue elements.

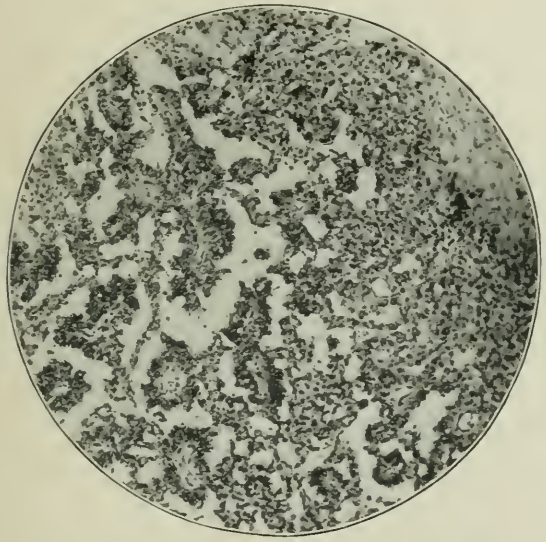

Fig. 3. Adenocarcinomatous and papillary tissue in a tumor which contains heterologous elements. Embryonal carcinoma of hypoblastic origin. Photomicrograph, × 80.

Of the latter, smooth muscle, cartilage, and glandlike or cystic spaces which are lined by well differentiated, single layered, cuboidal or columnar epithelium, the latter sometimes ciliated, are most frequent. It is from the epithelial structures, which are of a type which does not occur normally in the testis, that the atypical carcinomatous alveoli are derived. One tumor contains pigmented retinal epithelium, and two contain

masses of typical squamous epithelium. The teratomatous origin or mixed character of these tumors is established by their heterologous constituents.

In three of the nine tumors of adenocarcinomatous type no heterologous elements could be found in the material available for study. The atypical tissue, however, has the same character as that of the tumors which do contain heterologous elements. Because of this similarity it seems more reasonable to derive these

Fig. 4. Solid alveolar, carcinomatous tissue similar to that of basal cell carcinoma. Some of the areas of cellular tissue have a sarcomatous appearance. This tumor contains no definite heterologous elements; there are cysts lined by low cuboidal epithelium, from which the atypical epithelium is derived. Embryonal carcinoma of epiblastic origin. Photomicrograph, × 80.

tumors also from teratomas, than to accept a teratomatous origin for those which contain heterologous tissues and to suppose a different origin, from the tubuli recti, for example, for those which do not contain such tissues.

From a study of our material we are unwilling to accept the view that all of the malignant epithelial

tumors of the testis are of teratomatous origin. We believe that the solid, large cell, medullary tumors are derived from the spermatogenic epithelium of the seminiferous tubules, and that the tumors of a more adenocarcinomatous character are derived from teratomas. While, on the one hand, we cannot accede to the view of Ewing that all of the malignant epithelial tumors arise in teratomas, we cannot, on the other hand, see the necessity of deriving some of the tumors of carcinomatous nature from teratomas and others from the straight tubules, as do Frank, Sakaguchi, Geist and Thalheimer, and others. A dual origin of the human testicular carcinomas, as opposed to the single origin of Ewing or the multiple origin of others, is borne out by the incomparable Slye mouse tumor material. All of the atypical epithelial tumors of this material have been of the large cell type, which Slye, Holmes and Wells[9] derive from the seminal epithelium. None has been of the adenocarcinomatous type. What is more important, there have been no teratomas of the testis in this material. The nonoccurrence among these mouse tumors of two types of tumor, the teratoma and the adenocarcinoma, which occur so frequently in the human being, lends strong support to the view that the adenocarcinoma originates only in the teratoma and not in the straight tubules.

The histologic character of the malignant tumor of teratomatous origin may vary, depending upon the nature of the epithelial constituent of the teratoma which goes on to unrestricted proliferation. Most often it is epithelium of hypoblastic character which proliferates, resulting in a tumor of glandular or papillary type. In the next largest group the atypical elements have come from trophoblastic epithelium, resulting in the chorioma; in about half of the reported tumors of this kind, heterologous structures were present. Much rarer than either of the above is a solid, alveolar type of carcinoma similar to the basal cell carcinoma of the epidermis; tumors of this type may arise from the epiblastic constituent of a teratoma.

9. Slye, Maud; Holmes, Harriet F., and Wells, H. G.: Primary spontaneous tumors of the testicle and seminal vesicle in mice and other animals, Jour. Canc. Research, 1919, iv, 207.

In this connection attention is called to the recent publication of Heijl,[10] who believes that in the majority of all teratomas the atypical, carcinomatous tissue is epiblastic in origin and comes from neuroepithelial elements of the primitive central nervous system anlage.

A study of the age incidence of our tumors yields a striking point. Although the number of cases is too small to permit far-reaching conclusions, the relation of age to the two types of tumor is very suggestive and is a matter of importance in the clinical diagnosis if borne out by large numbers. In the six large cell tumors the average age is 41 years; in the nine adenocarcinomatous tumors it is 29 years. If a single tumor at the lower age limit in the first group is omitted, and two at the upper limit of the second group, the average ages are 42.6 years and 26.3 years respectively. The clinical duration of the large cell tumors arising at the higher age is shorter than that of the adenocarcinomatous tumors which arise at an average earlier age.

Summary.—Sarcoma of the human testis is a rarity. The name sarcoma should be discarded, unless the sarcomatous nature of any given tumor can be established beyond any doubt. The few undoubted spindle cell sarcomas which have been reported appear to have arisen in the tunics of the testis or epididymis.

The vast majority of malignant tumors of the testis are epithelial. These tumors fall into two main groups.

In one of these groups the atypical tissue is solid, medullary, and is composed of closely placed large polyhedral cells. It is to this type of tumor that the term sarcoma is so frequently misapplied. The large cell medullary tumor is derived from the germinal epithelium of the seminiferous tubules. For this tumor the name spermatocytoma is suggested.

In the second group of malignant tumors the atypical tissue has a glandular or papillary character. The majority of the tumors of this group contain heterologous tissues. All of the tumors of this group are probably teratomatous in origin. For this kind of tumor Ewing's designation of embryonal carcinoma may be retained.

10. Heijl, C. F.: Die Morphologie der Teratome. (Mit besonderer Berücksichtigung der Zentralnervensubstanz.) Virch. Arch., 1921, ccxxix, 561.

The embryonal carcinomas may be further subdivided according to the origin of the proliferating epithelial elements: hypoblastic (characteristically adenocarcinomatous); trophoblastic (chorioma); epiblastic (solid nonglandular alveoli of basal cell type, or rosettes of neuroepithelial origin).

In our series the spermatocytomas have all occurred at a later age period than the embryonal carcinomas of teratomatous origin.

Feb. 14, 1921.

FUSION DYSTOPIA OF THE KIDNEY WITH GENITAL ANOMALY

OSCAR T. SCHULTZ

From the Nelson Morris Memorial Institute for Medical Research of the Michael Reese Hospital, Chicago

In its embryologic development the tissue which gives rise to the permanent kidney passes through a complicated series of changes, some of which are progressive, others regressive. The origin of the urinary system is intimately associated with that of the genital system. The vascular relations in that portion of the body in which the urogenital system arises are quite different in early fetal life from those of later fetal and postfetal life; vessels which are prominent at the stage of development when the kidney is most susceptible to mechanical influences, later become small or disappear completely. This combination of circumstances makes the kidney liable to developmental anomalies which can be understood only upon the basis of embryogenesis. The urinary system anomalies may be associated with abnormalities in the genital system; the vascular supply of the abnormal kidney usually deviates from the normal; and there may be associated developmental errors in the terminal portion of the intestinal tract.

The embryologic data which have a bearing upon the the genesis of the congenital renal malpositions indicate the very considerable change in position which the fetal kidney must undergo before it reaches its permanent normal location. In this process the kidney

migrates from the caudal limit of the pelvic cavity to the cephalic limit of the abdominal cavity. According to the studies of Pohlman,[1] in the 4 mm. stage of the human embryo the lower end of the Wolffian body or mesonephric duct has reached and united with the relatively large cloaca. At 5 mm. the renal bud has been given off from the dorsolateral aspect of the Wolffian duct at a short distance cephalad to its cloacal end and lies near the caudal limit of the pelvic cavity; at this time the mesial surfaces of the two buds are only fifty microns apart. At about 10 mm. the renal bud has grown into the undifferentiated tissue lying ventral to the lower end of the aorta. This tissue later becomes the renal mesenchyme, from which the secretory portion of the kidney is developed. At this stage the two renal buds still lie very close to each other near the midline, behind the bladder in the sacral region, and are surrounded by the relatively large umbilical and postcardinal vessels and the Wolffian bodies. At about 14 mm. the kidneys lie opposite the midlumbar level. Axial rotation, which ultimately places the originally anterior or ventral hilum of the kidney on the mesial surface, has begun. The upward migration of the kidney, which is aided by regressive changes in the Wolffian body, continues, the normal renal level being reached at the 25 to 30 mm. stage of the human embryo. The vascularization of the kidney is effected after the organ reaches its permanent position.

In the permanent anomalies of position of congenital origin the kidney may be displaced in a vertical or in a horizontal direction. The anomaly may be unilateral or bilateral; it may be homolateral or contralateral; it may involve the single kidney when the other is absent; the malposition may be associated with fusion of the two kidneys. The case presented illustrates one type of the last named anomaly, i.e., fusion of the two kidneys with abnormal position of that portion of the fused mass which represents one of the kidneys. We

1. Pohlman, A. G.: Concerning the embryology of kidney anomalies, Am. Med., 1904, vii, 987. Abnormalities in the form of the kidney and ureter dependent on the development of the renal bud, Johns Hopkins Hosp. Bull., 1905, xvi, 51. A note on the developmental relations of the kidney and ureter in human embryos, Johns Hopkins Hosp. Bull., 1905, xvi, 49.

are dealing, therefore, with two different kinds of anomaly, fusion and dystopia, which need not be but sometimes are combined.

The most common fusion anomaly is that which results from union of the lower poles of the two kidneys and is associated with little or no abnormality in position, causing the typical horseshoe kidney. The form of fusion anomaly in which a kidney in normal position is fused with its mate, the latter being drawn partly or completely across the midline, ranks next in frequency to the horseshoe kidney. In this condition the fusion is associated with crossed dystopia; often a varying degree of vertical dystopia is also present in the misplaced kidney. More often the left kidney is misplaced, the right being in normal position. If the fusion has occurred by the lower poles, the displaced kidney lies at a lower level than the other and transversely across the midline (Fig. 1). In other cases there is a greater degree of lateral dystopia and less vertical dystopia, the posterior surface of the misplaced kidney being completely fused with the anterior surface of its mate. The result is a large, globular or "hog backed" kidney with a double pelvis from which two ureters are given off; one of these crosses the midline and empties into the bladder on the side opposite the kidney. It is this normal ureteral relation which differentiates such a fusion anomaly from a reduplication anomaly with true absence of the opposite kidney. Examples of this type, which are rare, are reported by Hill,[2] Felty,[3] and Huntington.[4] In the 25 recorded cases of fusion dystopia tabulated by McMurrich (quoted by Huntington), the right kidney was misplaced in 40 per cent., the left in 60 per cent.; of 23 cases, 78 per cent. were males and 22 per cent. females.

The misplaced portion of a fused kidney usually has the anomalies of vascular supply which are char-

2. Hill, E. C.: On the embryonic development of a case of fused kidneys, Johns Hopkins Hosp. Bull., 1906, xvii, 115.

3. Felty, A. R.: Bean-shaped double kidney—a rare type of dystopia and fusion, Jour. Urol., 1918, ii, 421.

4. Huntington, G. S.: The genetic interpretation of the variations in the genito-urinary tract, The Harvey Lectures, 1906-7, p. 222. J. B. Lippincott Co., Philadelphia, 1908.

acteristic of dystopia alone. Fusion with dystopia may be associated with the same genital anomalies as occur in dystopia without fusion or in absence of the kidney. As a rule the malformation of the genital system involves the efferent portion of the system rather than the gonads or the external genitalia. Fusion of the kidneys, with or without dystopia, is probably due to the same mechanical factors which act to produce dys-

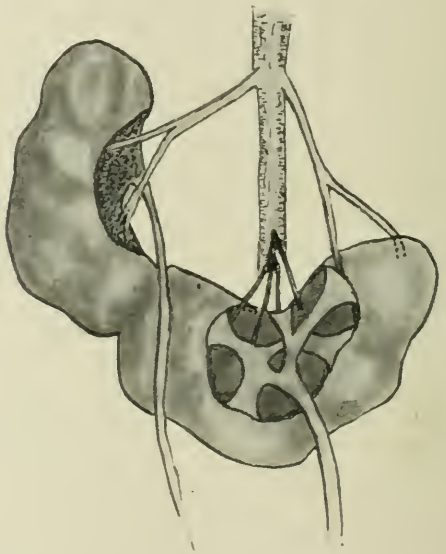

Fig. 1. Congenital fusion dystopia of the kidney. The transverse portion of the mass is the left kidney.

topia alone. Whether fusion occurs depends upon the proximity of the embryonic kidneys to each other at the time the mechanical factor is active. Bryan[5] believes that as the kidney moves cephalad it attains a new, temporary blood supply at each higher level, those vessels which were developed at the preceding lower level disappearing. If the temporary vessels do not

5. Bryan, R. C.: A case of Dietl's crisis in an anomalous right kidney associated with a left pelvic kidney, Surg., Gyn. & Obst., 1915, xxi, 684.

disappear the kidney remains stationary, anchored by the abnormal vessels which become permanent. This explanation is a simple one and fits in with the abnormal vascular supply of the dystopic kidney. But according to the work of Pohlman [1] and others, the kidney does not receive its vascular supply until it reaches its permanent position. The abnormal vascularization of the misplaced kidney would, therefore, be the result rather than the cause of the anomaly of position. Interference with the ascent of one kidney, the migration of the other occurring normally, appears to explain those cases in which the misplaced kidney is dragged partly across the midline by its mate. Complete fusion of the two kidneys, the fused mass attaining the normal position of one of the kidneys, is due to fusion without interference with ascent. Incomplete ascent of the kidney is usually associated with incomplete rotation in the long axis of the kidney. As a result, the hilum of the dystopic portion of a fused kidney is usually anterior and a normal pelvis is not formed, the ureter arising by union of separate calyces.

The case presented is a male infant from the maternity service of the Michael Reese Hospital. Delivery was normal and occurred two weeks before the calculated termination of a normal pregnancy. The infant gave a few feeble gasps after birth, but respiration was not established. There was nothing in the parental history which might have a bearing on the anomalies which were found to be present. As is so frequently the case, there are numerous developmental anomalies, in addition to those of the kidney. The associated genital anomalies are more extensive than is the rule in renal maldevelopments. The complete list of anomalies, which reads like the catalog of an anatomic museum, is as follows: absence of the middle finger of each hand; deformity of nose and left ear; atresia ani; absence of the penis; absence of testis and epididymis of left side; fusion and dystopia of kidneys; malformation of stomach; displacement of common bile duct; incomplete lobation of both lungs; single arterial trunk of heart; open foramen ovale; open septum ventriculi; talipes calcaneus of right foot; talipes calcaneovarus of left foot. Only those conditions which relate to the urogenital system will be described.

Kidney.—The two kidneys form a single fused mass of incomplete horseshoe shape (Fig 1). The right portion of the mass, which corresponds to the right kidney and has the normal position of the right kidney, is marked off from the rest of the mass by a faint shallow groove, which runs over the anterior surface of the mass 1.8 cm. to the right of the midline. The portion to the left of this groove is apparently the left kidney, which is displaced downward and lies with its long axis transverse to the longitudinal axis of the body. The fusion has occurred between the lower poles of the kidneys. The superior portion, corresponding to the right kidney, measures 4 by 1.5 cm.; the transverse portion, corresponding to the left kidney, is 4 by 2 cm. The latter portion lies opposite the promontory of the sacrum, its upper margin being just above the bifurcation of the aorta. The pelvis of the right renal portion of the mass has a normal position along the mesial border of this portion. The ureter runs downward over the anterior surface of the fused mass and ends in the bladder at the normal position of the right ureter. The hilum of the transverse portion of the mass occupies the anterior, upper portion of that part of the mass which corresponds to the left kidney. Five calyces unite to form the ureter; the latter takes a downward course over the anterior surface of the kidney slightly to the left of the midline and ends in the bladder at the normal position of the left ureter. The right kidney is supplied by a normal renal artery which divides into two branches before reaching the kidney, these branches entering the kidney at the upper and lower margins of the pelvis. The left renal artery runs downward and divides into two branches, one of which enters the posterior surface of the left end of the transverse kidney mass, the other the anterior surface at the left margin of the renal hilum. These vessels enter at that portion which corresponds to the upper pole of the left kidney. At a distance of 1.5 cm. above the bifurcation of the aorta a middle branch is given off, which divides immediately into four branches. These enter the hilum of the transverse portion of the mass. The veins run with the arteries. The bladder is small and apparently normal. Both seminal vesicles are present and the prostate appears normal.

Genital Apparatus.—Certain of the anomalies of the genital system are already apparent on external examination. The anus and penis are absent. Occupying the situation of the external genitalia is a pouchlike structure, which resembles a scrotum. The left half of this is small and empty. The right half is larger and in it a testis can be palpated. In the midline of the posterior border of the scrotum is a small

opening through which a small probe can be passed into the bladder. The right half of the scrotum contains a testis of normal size. This has a normal epididymis from which the vas can be traced upward through the inguinal canal. The left testis is absent and nothing corresponding to epididymis or vas can be found.

Adrenals.—These are normal in size and shape. The right has its normal position, closely applied to the upper pole of the right kidney. The left is slightly lower than the right and is separated by a considerable space from the left pole of the renal mass.

DUCREY BACILLUS INFECTION (CHANCROID) OF THE FACE

D. J. DAVIS AND H. W. POTTS

A negro 23 years of age came to the Cook County Hospital complaining chiefly of a painful swelling beneath his chin which began five days ago. It was marble sized when he first noticed it, gradually growing larger and more painful. It was because of this painful lump under his chin that he came to the hospital for treatment.

In addition to the above, he gave the following history. Two years ago he had a chancre and had had several attacks of gonnorhea at various times. Two weeks ago he developed a sore on his genitals and stated that after handling this lesion he remembered having scratched a small pimple on his chin.

When he entered the hospital genital examination revealed a typical chancroid of the penis of two weeks' standing and a definite inguinal lymphadenitis.

Upon his chin to the left of the median line was a small raised lesion which when the crust was removed revealed a ragged punched out ulcer ½ cm. in diameter whose floor was covered with a dirty grey exudate. He said it had existed for four or five days and was growing larger. Its base was slightly infiltrated and not very painful when compressed.

In the submental region, well forward, was a very painful, firm, movable tumor whose general contour was round and was about 5 to 6 cm. in diameter.

The scalp, ears, nose, eyes, tongue and throat were negative. His mouth was unclean and the lower left bicuspids were pulpless and decayed.

During the ensuing five days the lesion on the chin enlarged to 1 cm. in diameter and had ragged edges with some exudation which tended to form abundant crusts. The submental tumor increased in size and became soft and very tender.

Blood examination gave 5,280,000 reds, 11,000 leucocytes and 95 per cent. hemoglobin. The highest temperature recorded was 100 F.

With reference to the submental tumor, at first it was thought that a lymph adenitis might have developed from the decayed bicuspids as foci. This would have been unusual, however, since the lymphatics which drain the bicuspid region course farther back beneath the angle of the jaw. The presence of a genital chancroid, a lesion on the chin quite like the genital one, and the painful and progressive regional lympadenitis therefore seemed to warrant a tentative diagnosis of chancroid of the chin with submental bubo.

Crystals of argyrol were applied to the lesion on the chin, which promptly healed. The submental bubo softened and in a few days developed into a large abscess which was incised and the cavity packed with iodoform gauze. Recovery was uneventful.

The content of the abscess was examined bacteriologically. It contained many pus cells necrotic tissue and much blood. In stained smear preparations no bacteria were found even on prolonged search.

Suspecting the presence of B. ducreyi, the material was cultured in blood. For this purpose six small tubes containing about 2 c.c. of fresh human defibrinated blood were prepared and each inoculated with diminishing amounts of the material. Heavy blood agar tubes also were inoculated. After incubation the tubes were examined and in three of the six, growths of B. ducreyi appeared. A few staphylococci albus grew in some of the tubes but not in all. It was impossible to state whether or not they were contaminators or secondary invaders; probably the former, since they were not found in all the tubes.

The bacilli after twenty-four to forty-eight hours' growth appeared in typical tangled clusters of streptobacilli. Many also appeared in short and long chains. On superficial examination morphologically they resembled growths of streptococcus viridans. They are short oval bacilli, stained with difficulty by methylene blue and were gram negative. On solid media they form small grey, opaque colonies ½ mm. across, which appear in twenty-four hours and grow to maturity in two days. On plain media they gave no growth.

That the Ducrey bacillus is the specific cause of chancroid there can be no doubt. Ducrey in 1889

made fifteen successive human inoculations with material from the lesion, finally obtaining a chancroid in which practically only the streptobacilli were seen. He did not then know how to grow it. This was done by Lenglet in 1898, who cultivated it on human skin agar covered with blood. Heavy blood media or pure blood, defibrinated or not, have now come into general use in growing it.

At least three workers, Fischer, Lipschütz and Tomasczewski have inoculated themselves with pure cultures and caused typical chancroids. Monkeys are susceptible; also the cornea of the rabbit..

Extragenital chancroids are not uncommon on the lower part of the body, but rare about the head and face. In Kolle-Wassermann's *Handbuch,* Stein quotes Petersen as having observed twenty-seven extragenital lesions in a series of 9,000 chancroids. Ullmann collected from the literature and his own experience sixty-four extragenital chancroids. Of these, forty-nine had both genital and extragenital lesions (as in the case here reported); twenty-two were on the fingers. Of chancroids in other localities, one has been reported on the gum of the upper jaw, two on the conjunctiva, one on the tonsil, one on the tongue, one on the soft palate and wall of the pharynx and one in the external auditory canal. None on the chin or face was found reported.

March 14, 1921.

THE RELATION OF CHEMICAL COMPOSITION TO IMMUNOLOGIC SPECIFICITY

H. GIDEON WELLS

Two distinct lines of investigation have been followed by numerous workers in studying the relation of chemical constitution to immunological specificity. One developed especially by Obermayer and Pick, and by Landsteiner has consisted in producing chemical alterations in the protein molecule by addition of various chemical groups. These studies have shown

that proteins can be so modified that their immunologic specificity is greatly changed and the relations of the derived proteins are found to correspond immunologically and chemically. Similar conclusions have been reached by the method of using purified proteins, comparing the immunologic results with the chemical constitution of the proteins. Both methods show that immunologic specificity is not a function of biochemical origin of proteins but depends entirely upon the chemical constitution of the proteins. Proteins of identical biologic origin chemically distinct are likewise immunologically distinct, whereas proteins of diverse biologic origins but with chemical similarity show immunologic similarity or identity. Casein of milk, for example, seems to show close immunologic relation no matter from what species it is derived.

A study of the chemistry of the proteins of milk by Dr. T. B. Osborne has been accompanied by a study of the antigenic properties of the same proteins and has demonstrated that wherever chemical methods show different protein fractions of the milk to consist of chemically distinct proteins they show corresponding immunologic distinctions. It has been found possible to use the anaphylaxis reaction to control the chemical study of proteins, since information concerning the nature of a given protein is furnished by very small quantities of the material. It has been possible to identify four chemically and immunologically distinct proteins in cows' milk, namely, casein, lactabulmin, lactoglobulin and an alcohol soluble protein newly discovered by Osborne. Although all derived from the same secretion, they can be sharply differentiated by the anaphylaxis reaction. They are all immunologically distinct from beef serum with the exception of the globulin, which sensitizes well to beef serum and conversely. Probably it corresponds to the globulin fraction of beef serum. This explains the fact that whole cows' milk gives especially strong reactions with beef serum, since colostrum contains many times as much globulin as the later milk.

(The full details of this work are published in the *Journal of Infectious Diseases*, 1921, vol. 29, p. 200.

March 14, 1921.

THE OCCURRENCE OF SQUAMOUS CELL CARCINOMA IN MICE

MAUD SLYE, HARRIET F. HOLMES AND H. GIDEON WELLS

The literature on the comparative pathology of carcinoma shows that in general squamous carcinomas are not so common in other animals as in man, with the possible exception of the dog, in which carcinoma of the skin is not infrequent. This infrequency in animals is probably more real than the statistical figures indicate, since the skin carcinoma will usually be recognized, whereas the great majority of internal growths will escape attention. In horses, carcinoma of squamous character about the external genitalia of both sexes is seen occasionally. Fowls and other birds not infrequently show carcinoma of the skin, and such growths have also been observed in fish and amphibia. A few tumors of this group have been described in rats or mice. A few tumors of the mouth and skin have been observed in mice as well as a few cases of squamous cell carcinoma arising from the cardiac end of the stomach. Most of the squamous cell carcinomas described in mice have occurred in the mammary gland apparently arising either from the ampullae of the lacteal ducts or by metaplasia of the columnar cell carcinoma.

In 28,000 consecutive autopsies performed on mice of the Slye stock, which had been permitted to live as long as possible without any experimental manipulations whatever, we have observed the following instances of primary neoplasms of squamous or stratified epithelial structure.

Primary squamous cell carcinoma of the skin and mouth, 71; primary basal cell carcinoma of the skin, 15; primary keratinizing cell carcinoma of the mammary gland, 56; primary squamous cell carcinoma of the stomach, 4; primary keratinizing cell carcinoma of the lung, 1; primary squamous cell carcinoma of the rectum, 2; primary squamous cell carcinoma of the

vagina, 1; primary stratified carcinoma of meibomian gland, 2; primary sebaceous gland adenocarcinoma, 1. Total, 153.

The squamous cell carcinomas of mice are distinguished especially by the infrequency of metastasis and they generally show a relatively slight tendency to infiltrate, although we have observed even infiltration of the skull and spinal column. This probably depends on the fact that secondary infections usually kill the mice at an early stage of the disease. All the basal cell carcinomas and the great majority of squamous carcinomas arose about the head, neck and mouth, these being the sites of the greatest amount of irritation. Frequently they have arisen in healed wounds.

(A full report of this material is published in the *Journal of Cancer Research*, 1921, vi, 57.

March 14, 1921.

REPORT OF AN INTRAVASCULAR TUMOR, PROBABLY A SPINDLE-CELL SARCOMA

ANFIN EGDAHL

From the Johnson Clinic, Rockford, Ill.

This tumor is reported as it may have a bearing on the old question of the nature of primary intravascular tumors. Are all or none endotheliomata? Or have we primary endotheliomata and primary sarcomata, or primary tumors of other types of cell structure occurring intravascularly? All these views have had their advocates. The following case has been a very interesting subject for study, as it presented unusual features as to history and also as to pathologic findings.

CASE HISTORY

Family History.—No history of tuberculosis, cancer, nervous diseases, or any diseases that resembled syphilis.

Personal History.—Has always enjoyed good health. No history of syphilis or gonorrhea.

Present Illness.—Nine years ago noticed a nodule on front of right wrist near middle line. This was about the size of a pinhead and was freely movable. At end of first year, it had attained the size of a pea; at end of second year, it had doubled in size. The tumor grew steadily until about two years ago, when it had attained the size of a golf ball. Since then, it has grown rapidly and has shot out a long tortuous branch, extending nearly to elbow which in turn has smaller tortuous branches. One of these smaller branches extends up over back of the thumb. There has been no pain or any inconvenience of any kind until two weeks ago, when the wrist began to ache and the forearm began to show a reddish-bluish color.

Examination.—A general examination, including the sense organs and reflexes, reveals nothing abnormal. An examination of the tumor shows a mass on anterior aspect of right wrist, about the size of a small apple. From this a thick tortuous branch extends up over forearm almost to elbow. This, in turn, has several smaller tortuous branches, one of which extends up over back of the thumb. No pain is produced on pressure and no pulsation is felt. The overlying skin is of a reddish-bluish color. No enlargements of epitrochlear or axillary glands is noticed, or of any other lymphatic glands. A complete blood examination, including a Wassermann test, was negative. A roentgenogram was taken of forearm, wrist and hand to see if there was any possibility of involvement of bones, but this was negative.

Judging by the history, a diagnosis of a malignant tumor was made, and an operation was advised. Dr. T. A. Johnson operated and was surprised at the ease with which the tumor was removed. A portion of the base extended deep into the wrist, but this shelled out just as easy as the rest of the growth. The tumor was found to be composed of veins filled with a firm, solid growth, but toward the tapering points the growth slipped easily out of the veins, as a finger out of a glove.

Gross Pathology.—The tumor presented a most curious appearance, resembling somewhat the body and radiating arms of a small cuttlefish. The total length is 29½ cm. The length of body or main portion of tumor is 7½ cm. and its width at the widest portion is 4½ cm. The length of the main branch is 22 cm. There are three smaller branches, springing from the main branch, being respectively 4 cm., 5½ cm. and 4½ cm. in length, counting from the body. From these, in turn, spring one or more shorter branches. The width of the main branch at its widest portion is 1½ cm. This tapers gradually to a blunt point about ½ cm. in

width. Along its course are a few nodules. The first side branch is 1¼ cm. in width and tapers rapidly to an obtuse point. It, in turn, has two small side branches. The second branch is nodular in appearance and has two short branches. The widest nodule is 2 cm. in width. The third branch tapers gradually to a blunt point ⅛ cm. in width. This, in turn, has two small branches. The body of the tumor has a mottled appearance, being in places of a bluish color, in other places, grayish in color; evidently, the blue areas are caused by an accumulation of blood underneath the capsule of the growth. This bluish color extends in places up the main branch of the tumor, but aside from this the grayish color is the predominant color present. The whole tumor is of a firm elastic consistency. The entire growth is covered by a glistening capsule. On the branches, this can be stripped off easily, but on the greater surface of the body it seems to be firmly adherent. At the cut ends of the smaller processes it can be stripped back like a cuff. On cutting into the main body of the tumor from above downward, the knife passes first through the membrane and the adherent tumor mass, then through an area containing small blood vessels filled with blood, then into a cavity, filled with blood, running the length of the main tumor mass. This cavity varies from ¼ to ½ cm. in width and is bounded below by the capsule, which is evidently the wall of a vein. The same firm elastic consistency and grayish color is noticed in the growth as described before. Sections made in the branches also show the same appearance and consistency but no accumulation of blood is noticed, aside from that in small blood vessels in the tumor tissue itself.

Microscopic Examination.—Sections from different parts of the growth were examined. All showed as the predominant cell a spindle-shaped cell. These cells were arranged in twisted bundles, which ran in different directions, so that in any given slide cells could be seen in cross section or in longitudinal section. The outline of these cells was not sharp. The protoplasm was of a uniform consistency, while the nucleus appeared to be finely granular, and in most sections showed a well defined nucleolus. The nucleus was fairly large; mitotic figures were not numerous. In the older part of the tumor considerable degeneration was in evidence in various places, particularly toward the center of the tumor. In all parts of the growth new-formed capillaries can be found, and a thin delicate stroma is present in a number of the sections examined. The capsule is found to show the histologic characteristics of a vein. It is evident, then, that we have to deal with an intravascular

tumor. On close examination of the older part of the growth, it is found that the tumor has taken its original from the wall of a blood vessel. Since this is the case, the question as to whether this tumor should be classed as an endothelioma or not at once becomes evident. I have gone over the literature of about fifteen so-called intravascular endotheliomata, several of which duplicated the case in question. My first diagnosis was that of spindle-cell sarcoma, but later I was for a time inclined to consider this case an endothelioma, basing my diagnosis on the history and the possibility of pressure of the confined cells within the vein, causing the cells to take on the spindle shape so evident in the sections, and on the faculty possessed by the endothelial cells to assume the characteristics of fibroblasts. On further investigation, and after having obtained the opinion of Professor Zeit, I came to the conclusion that the most probable diagnosis was spindle-cell sarcoma, and that the site of origin was in the wall of the vein. Cells were found that could be called endothelial cells, but when two or more tissues are present in a tumor, it is necessary to decide their relative importance, or if one or more represents metaplasia or degenerative changes in the other.

MacCallum states that it is unfortunate that many tumors, whose origin and histogenetic relations are difficult to trace, are classed under endotheliomas, especially if they occur in unusual sites. In practically no case has the origin of a tumor from endothelium been proven. Ribbert states that the continuity of the tumor with endothelium is not proof enough. It is also possible for a tumor growing into channels to stimulate the endothelium to growth, as in the case of a foreign body, but this does not necessarily mean their participation in the tumor growth. As far as I have been able to ascertain, Golgi was the first to give the name of endothelioma to these growths within blood and lymphatic vessels. This was in 1869. Since then, a number of contributions to the literature of intravascular growths have been made, particularly by Borman, Ravenna, Duffard, MacCallum, Waldeyer, Zeit and Ribbert.

Duffard believes that endothelial cells of blood vessels may give rise to intravascular endothelial tumors. Ravenna believes that the reason for the great difficulty in making a definite diagnosis is due to the fact that

these tumors are scarcely ever seen at an early stage. Nevertheless, in the tumor in question, the histologic characteristics favor the diagnosis of spindle-cell sarcoma so strongly that the only possibility of its being an endothelioma would be on the assumption that the endothelial cells has assumed the shape of spindle cells and appeared as fibroblastic elements, which they may at times do. A study of sections from different parts of the tumor would not, however, warrant the statement that this had taken place here. There was no evidence of mucoid or amyloid degeneration so characteristic of endotheliomas. Clincially speaking, the diagnosis would now seem to favor a spindle-cell sarcoma. Zeit states that an endothelioma is not so likely to metastasize as a sarcoma, but is more likely to recur locally after removal. In this case, it has not recurred locally, but within the last month, one year after removal, a small, firm growth has developed on the angle of the right lower jaw. This is perfectly painless and has been of slow growth.

CONCLUSIONS

1. This tumor is an intravascular growth, showing as the predominant cell a spindle-shaped cell. There are a few cells present which have the appearance of endothelial cells. However, the diagnosis of this growth as an endothelioma would be justified only on the assumption that the cells had assumed the shape of spindle cells, and appeared as fibroblasts.

2. In my opinion, we are dealing with an intravascular spindle-cell sarcoma of the large cell type, taking its origin in the wall of a vein. This view is strengthened by the appearance of what may be a metastatic nodule at the angle of the right lower jaw. A roentgenogram of the chest shows a nodule of fair size to the left of the hilus. This nodule is somewhat larger than the usual peri-bronchial lymph-node of a chronic tubercular infection, and may possibly be a metastatic nodule.

March 14, 1921.

MYELITIS AND MYELOMALACIA

PETER BASSOE AND GEORGE B. HASSIN

Lantern slide demonstration of the histologic changes in the spinal cord in a case of softening in the thoracic region following so-called acute myelitis. The patient died four months after the onset. An especial effort was made to point out the part played by various cells of glia origin, such as gitter cells and myelophages.

(The complete clinical and pathological report will be found in the *Archives of Neurology and Psychiatry, 1921.*)

March 14, 1921.

THE IMMUNOLOGIC REACTIONS OF FIVE STRAINS OF BACILLUS INFLUENZAE ISOLATED FROM A CASE OF MENINGITIS

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Huntoon and Hannum,[1] as the result of agglutinin and absorption experiments, found a close relationship between strains of influenza bacilli. Small and Dickson [2] also found strain relations by agglutination methods and placed their strains in four groups. Opposed to these findings, based upon a relatively small number of strains, are the results of Valentine and Moore,[3] Utheim,[4] Bell,[5] Cooke,[6] and others, which are based on the study of a very large number of strains. The latter workers could find no evidence of strain identity by immunologic methods and concluded that under the name B. influenzae is included a very hetero-

1. J. Immunol., 1919 (4) 167.
2. J. Infect. Dis., 1920 (26) 230.
3. J. Immunol., 1919 (4) 359.
4. J. Infect. Dis., 1920 (27) 460.
5. J. Infect. Dis., 1920 (27) 464.
6. J. Infect. Dis., 1920 (27) 476.

geneous group of organisms. When more than one strain was isolated from one individual the strains might be identical or they might be quite distinct. The work thus briefly summarized was done on strains isolated chiefly from the respiratory tract. The isolation of five strains of influenza bacilli from a case of meningitis gave an opportunity for investigating the question of immunologic similarity or dissimilarity on the basis of strains derived from the same individual, two of which were definitely invasive, and all of which might *a priori* be supposed to be related to each other. A detailed report of this study has already been published.[7]

The patient was a white, male infant aged 17 months, who was admitted to the service of Dr. I. A. Abt in the Sarah Morris Hospital for Children; the admitting complaints were vomiting, generalized muscular twitching, rigidity of the body, fever, discharging right ear, and strabismus. The illness had begun with fever and vomiting four days before admission; muscular twitching appeared two days and rigidity one day before admission; strabismus developed on the day before admission. Death occurred on the seventh day in the hospital. The first culture of B. influenzae was obtained from spinal fluid removed on the day of admission. This fluid had a cell count of 3,500 and all the characteristics of a fluid from acute purulent meningitis. On the following day cultures were made from the nose, throat, nasopharynx, ear and blood. Typical colonies of B. influenzae appeared on blood agar cultures from the nose, throat, nasopharynx, blood and spinal fluid, but not from the ear; the ear cultures gave only a pure growth of *Staphylococcus albus*. From spinal fluid removed on the next day after admission, when the cell count had increased to 10,000, B. influenzae was again obtained in pure culture. Subcultures from selected colonies of the first spinal fluid culture and of the nose, throat, nasopharyngeal, and blood cultures were used for study.

Pathogeneeity.—Rabbits injected with the strains isolated from the blood, throat and nasopharynx died

7. J. Exp. Med., 1921 (33) 653.

within twenty-four hours after one injection. In each case influenza bacilli of typical morphologic and cultural characteristics were isolated from the heart's blood. Rabbits which were inoculated with the strains from the nose and spinal fluid lived and were used for further immunization.

Immunization.—For the production of immune serums rabbits were used. The animals were immunized by intravenous injections which were repeated every other day. There were prepared two serums against the same spinal fluid organism, and one serum against each of the other strains. These serums were used for a study of agglutination, complement fixation and phagocytic activity.

Agglutination.—The macroscopic method was used. Each immune serum was set up in dilutions increasing

TABLE 1.—AGGLUTINATION

Suspensions of *B. pfeifferi*	Immune Serums						Normal
	Spinal Fluid 1	Spinal Fluid 2	Blood	Nose	Throat	Naso-pharynx	Rabbit Serum
Spinal fluid....	1: 4,096	1: 1.024	1: 64	1: 64	1: 64	1: 16	0
Blood	1: 8	1: 32	1: 128	1: 4	1: 4	1: 4	0
Nose	1: 64	1: 128	1: 32	1: 64	1: 32	1: 8	0
Throat	0	0	0	0	1: 1.024	0	0
Nasopharynx ..	1: 64	1: 64	1: 16	1: 256	1: 8	1: 512	0

by geometric progression with its homologous strain and with the four heterologous strains. To each dilution of serum an equal quantity of bacterial suspension was added, the total volume of fluid being 0.5 cm. Incubation at 37 degrees for two hours, followed by standing over night in the cold storage room, gave better results than incubation at higher temperature. Fresh living suspensions of twenty-four hour cultures agglutinated better than older killed suspensions. The results of the agglutination tests are given in Table I, the figures being the highest dilution of serum at which clumping was visible to the naked eye.

With the exception of the serum against the strain from the nose each serum agglutinated best with its homologous strain, but there was a wide variation in the titer of the serums for their homologous strains. Cross agglutination occurred, but only in low dilutions of

serum, when the heterologous strains were used. The serums against the spinal fluid strain had a much higher titer than the other serums. Absorption experiments could not be done because of the exhaustion of the supply of serums and of the loss of the strains. The results of the agglutination experiments indicate distinct differences between the five strains.

Complement Fixation.—Undiluted immune serums heated at 56 degrees for thirty minutes were used. The system employed was the antisheep-rabbit in one-

TABLE 2.—COMPLEMENT FIXATION

Antigens of *B. pfeifferi*	Immune Serums						Normal Rabbit Serum
	Spinal Fluid 1	Spinal Fluid 2	Blood	Nose	Throat	Naso-pharynx	
Spinal fluid	1/256	1/256	1/4	1/64	1/128	1/64	1/4
Nose	....	....	....	1/64	....	....	1/4
Throat	....	....	....	....	1/64	....	1/4

TABLE 3.—COMPLEMENT FIXATION

Antigens of *B. pfeifferi*	Immune Serums						Normal Rabbit Serum
	Spinal Fluid 1	Spinal Fluid 2	Blood	Nose	Throat	Naso-pharynx	
Spinal fluid	1/32	1/128	1/8	1/16	1/32	1/16	1/8
Blood	1/8	1/8	1/8	1/8	1/8	1/8	1/8
Nose	1/32	1/32	1/16	1/64	1/64	1/16	1/8
Throat	1/32	1/32	1/8	1/32	1/32	1/32	1/8
Nasopharynx	1/32	1/32	1/32	1/16	1/16	1/32	1/16

tenth the volume of the original Wassermann reaction. Serum and complement were kept constant. The antigen quantities were varied, the figures given in Tables II and III being the fractions of the anticomplementary unit which gave complete inhibition of hemolysis.

In the experiments tabulated in Table III, the serums used were obtained, after exhaustion of the original supply, by reimmunizing the original rabbits with stock killed suspensions which had been prepared at the beginning of the work; the same stock suspensions were used as antigens. In the experiments of Table II, the spinal fluid, nose and throat antigens were freshly prepared, unheated suspensions, and the serums

were of the lot originally prepared and used for the agglutination experiments.

As has been found to be the case with other bacterial species, complement fixation gave less specific and clear cut results than did agglutination. The complement fixation results were, furthermore, somewhat unsatisfactory because all of the normal rabbit serums tried gave some fixation with the various bacterial antigens; this nonspecific fixation was greater with the older stock suspensions than with the fresh ones.

Opsonins.—The action of the immune serums in increasing the phagocytic activity of rabbit leukocytes was studied by mixing equal parts of suspensions of living bacilli, normal rabbit leukocytes and inactivated

TABLE 4.—OPSONINS

Suspensions of *B. pfeifferi*	Immune Serums: Spinal Fluid 1	Spinal Fluid 2	Blood	Nose	Throat	Nasopharynx
Spinal fluid	2.1	1.9	...	...	...	...
Blood	...	...	1.4	...	...	...
Nose	...	...	...	1.8	...	...
Throat	...	...	...	...	1.5	...
Nasopharynx	...	...	...	...	...	1.6
Blood	1.3	1.2	1.4	1.1	1.0	1.0

serum. The mixtures were incubated at 37 degrees for thirty minutes. Fifty polymorphonuclear leukocytes were counted and the number of cells which had taken up bacilli was compared with a similar series in which normal rabbit serum replaced the immune serums. The strain isolated from the blood was set up with all the serums, the other strains only with the homologous serums. The results are given in Table IV.

The opsonin experiments show much the same kind and degree of variation as the agglutination tests. The spinal fluid serums, which had the highest agglutinin titers, had also the greatest opsonic activity.

The five strains isolated show distinct immunologic differences. The strains isolated from the nose and the nasopharynx show a greater apparent relationship than any other two strains, and there may have been

some slight degree of relation between the spinal fluid and nose strains. The relationship, however, is less marked than occurs among certain bacteria which are held to be distinct species. The probable course of events in the case from which the five strains studied were isolated would appear to have been an invasion of the meninges from the nose or nasopharynx, with later invasion of the blood stream from the meninges. It is believed that there must have been some direct genetic relation between these various strains. Although different strains, even from the same case, may show wide variations in experimental immunologic reactions, such strains are probably not as distinct from each other as are the various members of the colon-typhoid intermediate group. The subculturing of a larger number of colonies from the original cultures from the case studied might have yielded a still larger number of immunologically different strains.

Summary.—Five strains of influenza bacillus, isolated from the same case, a child with clinical acute meningitis, showed distinct immunologic differences. These strains were derived from the spinal fluid, blood, nose, throat and nasopharynx. Although they were immunologically distinct, these strains are believed to have been genetically related. It would seem, therefore, that differences in experimental immunologic reactions among influenza bacilli cannot have the same value in determining relations or dissimilarities among strains as when these methods of study are applied to other groups of bacteria. The results on five strains isolated from the same case confirm those of those previous workers who could find no evidence of strain relationship. The explanation of the differences among strains which must be, as in the case of the five here reported, actually related to each other, is a matter for further study. Whether these biologic differences have any bearing on the causal relation of B. influenzae to the epidemic disease must remain for future investigation to determine.

April 11, 1921.

RUPTURE OF AN ANEURYSM OF THE ASCENDING AORTA INTO THE SUPERIOR VENA CAVA

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But 43 instances of rupture of an aneurysm of the ascending aorta into the superior vena cava are found in the literature, and this case is reported in order to add it to this list. Pepper and Griffith [1] in 1890 found 29 cases, Fussel [2] in 1906 found 7 and Herrick [3] recently added 7, making the total, including this case, 44.

Points of interest in the clinical record of this case are briefly given below: An Irishman, aged 52 years, laborer by occupation, came to the Cook County Hospital, December 8, complaining of shortness of breath, swelling of the face and neck with blueness, and cough. About five weeks previous to admittance he had to stop his work as a day laborer because his face became a little blue, the veins in his face and neck large, shortness of breath marked, and cough a little troublesome. About two weeks after this, he awakened one morning to find the cyanosis of his face more marked than before and the swelling more pronounced than it had been the night before. The swelling and cyanosis always increased when lying down or exercising, but there was no associated pain.

His past history records a chancre at 15 years of age, but no report of specific treatment. He was a chronic user of alcoholics, averaging four glasses of whisky daily. Negative points include, no visual disturbances, no swelling of the lower extremities, no pain in the chest, no vomiting, and no urinary disturbances.

Physical examination revealed an adult white man, only fairly well nourished, the size of whose head and fullness of face, neck and chest was all out of proportion to the rest of his body. He tended to fall asleep but awakened easily and talked with a little difficulty. His temperature was 97 F. by mouth, his pulse 80 and respirations 20 per minute. When

1. Pepper and Griffith, 1890, Transactions of the Association of American Physicians.
2. Fussel, 1906, Transactions of the Association of American Physicians.
3. Herrick, J. B., American Journal of Medical Sciences, pp. 158-782, December, 1919.

quiet the respirations were of the Cheynes Stokes type, there being deep breathing for 20 seconds and apnea for 20 seconds. The right brachial blood pressure was 126 systolic, and 40 diastolic—the left 116 and 40 respectively.

The skin of the face, entire head, neck, chest and arms, and the buccal mucosa were distinctly cyanotic. The eyelids, subcutaneous tissues of the face, head, neck, and chest were all distinctly waterlogged and pitted readily on pressure. The edema decreased from above downward and stopped at about the costal margin. There were engorged veins of the face, neck, chest and abdomen and the latter joined with the superficial epigastric veins. The flow of blood in them was apparently downward. Resonance over the lungs was increased and moist rales were heard over the base of the left lung.

The radial pulse had a quick rise and fall and was about equal in the two arms.

On inspection there was a visible pulsation of the left portion of the sternum opposite the third and fourth ribs. The apex beat was in the sixth interspace 2 cm. to the left of the nipple line. Percussion revealed the mediatinal dullness out about 3 cm. to each side of the normal limits. The right heart border was 2 cm. to the right of the right sternal border and the left border was at the anterior axillary line.

On auscultation there were three heart murmurs heard; one, a systolic murmur, not transmitted, was heard at the apex; a second loud whirring diffuse murmur like the stroke of a steam pump was present, loudest at the start of the systole, fading out gradually but continuing through diastole to the next systole; a third short diastolic murmur was heard immediately following the clear distinct second aortic sound.

The abdomen was soft, free from edema, palpable viscera or tumor masses. The lower extremities were thin and poorly nourished. The tendon reflexes were present and not abnormal.

The diagnosis made at this time by the intern, Dr. Walter Earle, was mediastinal tumor, probably aortic aneurysm, with obstruction to the superior vena cava or possible rupture into it.

Roentgen examination demonstrated a greatly dilated aortic shadow but no definite aneurysm and a little pleural effusion. The latter on thoracentesis had a specific gravity of 1010, was clear, straw color and contained a few lymphocytes.

The Wassermann test of the blood serum was strongly positive.

The urine contained albumin and a trace of bile.

The blood upon admission had a hemoglobin of 75 (instrument not recorded) 3,680,000 erythrocytes and 6,600 white cells. Twenty days later the hemoglobin was 65, the red cells 2,580,000 and the white cells 4,200.

Progress notes indicate that the patient was very restless at night and often wandered about the ward apparently out of his head. The edema and cyanosis increased as did the fluid in the pleural cavities and death occurred on January 17, forty days after admission.

NECROPSY

At the postmortem examination made about eight hours after death, the body was 160 cm. long and weighed 140 pounds. The upper half of the body was puffy from edema and markedly cyanotic, while the lower half was pale and emaciated. Engorged tortuous veins were present under the skin of the face, neck, chest and abdomen. A scar from a healed chancre could not be demonstrated on the penis by naked eye examination.

In the mediastinum in front the aortic area was widened to 12 cm. and the cardiac to 18 cm. The right auricle rested closely against the diaphragm below and had for its upper margin a large aneurysmal sac, which without close dissection was 14 cm. up and down, 10 cm. wide and 10 cm. front to back. The coronary veins and arteries were engorged with purple blood.

Opening the vena cava from behind it was filled with purple blood but had a smooth lining. The superior cava was compressed, begining at its mouth and for 10 cm. upward. Its greatest circumference was 9 cm. In the narrow place in the superior vena cava, and 4 cm. above its opening into the auricle, there was an oval 5 mm. opening, joining the lumen of the vena cava with that of the aneurysm. On the margins of the opening were grey pink fibrin masses, grossly not unlike small vegetations. The aneurysm was in the ascending aorta beginning at the aortic valve and extending to the transverse arch so that the only openings into it were the left ventricle, transverse aortic arch, and the small ruptured opening into the superior vena cava. The wall of the aneurysm was only ½ cm. thick and its lining was very rough from yellow to grey placques, surrounding which were linear furrows and depressed scars. The cavity of the aneurysmal sac admitted easily a large fist and its diameters in all directions were from 10 to 12 cm. Except for fibrous thickenings there were no changes of the heart valves, and the myocardium was pale and streaked with white fibrous tissue.

The coronary arteries were roughened from sclerosis. The empty heart, aorta and aneurysm together weighed 725 gm.

There was clear straw colored fluid in the pleural cavities, 4 liters in the right and 2 in the left. The lungs were boggy from edema and there was passive hyperemia of the viscera.

April 11, 1921.

A PATENT FORAMEN OVALE

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This specimen was taken from the body of a 10 months old white boy who was brought to Cook County Hospital on January 27 because of cough, vomiting and difficulty of breathing.

According to the mother the child had not been well since birth; having had a cough most of the time. In the two months previous to entrance he gradually became worse and dyspnea was noticed. Vomiting had been present from birth both between and immediately after nursing.

The baby was normally born, and breast fed for nine months, when supplementary feedings were started. He sat up at 3 months and his first tooth erupted at 5 months of age.

Physical examination revealed a fairly well nourished youngster who was restless and appeared acutely ill. His neck was stiff, but there was no opisthotomus. The temperature was normal, the heart was enlarged and there was heaving of the precordium, the L.H.B. was at the left anterior axillary line and the R. H. B. was at the right anterior axillary line. The tones were very rough. Loud murmurs, both systolic and diastolic, were heard everywhere over the cardiac area.

The only other changes noted were loud roles over the lungs but no dullness.

No changes were noted of the spinal fluid. Blood Wassermann was negative.

Roentgen examination revealed a marked enlargement of the heart, chiefly of the right ventricle and auricle.

The physical findings and roentgen-ray report prompted a clinical diagnosis of congenital pulmonary stenosis and interventricular defect.

Necropsy.—Postmortem examination was made about two hours after death. About one third of the lung tissue was solid from bronchopneumonia. The apex of the heart was round, and was made up of about twice as much of the right ventricle as of the left. The pulmonary valves and the other heart valves were entirely unchanged. The ductus arteriosus was closed. No defect of the wall between the ventricles was present. A patent foramen ovale 14 mm. in diameter was present and clotted blood extended through it. The walls of both ventricles were 9 mm. thick and the empty heart weighed 60 gm.

There was a moderate edema of the brain present.

April 11, 1921.

THE SPECIFIC PRECIPITIN REACTION OF THE LENS*

LUDVIG HEKTOEN

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It is a remarkable fact, discovered by Uhlenhuth and verified by others,[1] that the lens of different species gives the same immune reactions. A lens antiserum, produced, let us say, by injecting a rabbit or guinea-pig with beef lens, will react in precipitation, anaphylaxis and complement fixation tests not only with beef lens but also with the lens of other mammals, of birds and

* Printed in Jour. Amer. Med. Assn. **77**: 32, 1921.

1. Uhlenhuth: Zur Lehre von der Unterscheidung verschiedener Eiweissarten mit Hilfe spezifische Sera, Koch Festschrift, 1903, p. 49. Andrijew: Ueber Anaphylaxie mit Eiweiss tierischer Linsen, Arb. a. d. k. Gsndhtsamte **30**: 450, 1908. Kraus, Doerr and Sohma: Ueber Anaphylaxie durch Organextrakte (Linsen), Wien. klin. Wchnschr. **21**: 1084, 1908. Uhlenhuth and Haendel: Untersuchungen über die praktische verwertbarkeit der Anaphylaxie zur Erkennung und Unterscheidung verschiedener Erweissarten, Ztschr. f. Immunitätsf. u. exper. Therap. **4**: 761, 1909. Krusius: Zur biologische Sonderstellung der Linse, Ztschr. f. Immunitätsf. u. exper. Therap. **5**: 699, 1910; Ueberempfindlichkeitsversuch vom Auge aus, Arch f. Augenh. **67**: 6, 1910. Königstein: Zur Biologie der Linse, Arch. f. Augenh. **68**: 414, 1911. Römer and Gebb: Beiträge zur Frage der Anaphylaxie durch Linseneiweiss, Arch. f. Ophth. **81**: 367, 1912.

amphibians. With fish lens the reaction, however, is very faint. We see that the specificness of the reaction is determined not by species as in the immune reactions of blood, of serum proteins, as well as of bacteria, but by the organ from which the antigen is derived.

So far the lens is the only clean-cut example we have of this organ-specificness as contrasted with species-specificness in antigen-antibody reactions. In fact, so perfect is this lens-specificness that a lens antiserum reacts with the lens of the species, yes, even of the very animals, that furnishes the serum, but not with any other proteins, and antiserums produced by injecting animals with blood or serum do not react with lens solutions.

The observations on the immune reactions of the lens have been made by means of specific precipitation tests of lens solutions, study of the anaphylactic effects of reinjections of lens solutions in guinea-pigs previously injected or sensitized with such solutions, and complement fixation tests, associated of course in any case with proper control procedures.

I have studied the precipitins that develop in rabbits on the injection of lens solutions in 0.9 per cent. salt solution. The principal experiments so far have been made with approximately 10 or 20 per cent. solutions by weight of beef, horse, rabbit, sheep and swine lens, removed with special care to avoid admixture with blood or serum. Rat lens and chicken lens seem to be more toxic, but I have not studied that phase in detail. As a rule, four or five injections have been given intravenously at four day intervals, first of 2 to 4 c.c. of solution, increasing gradually to between 12 and 16 c.c. the last time. The highest precipitin titer of the serum after such treatment appears to be reached about the eighth day after the last injection. Contrary to the experience of Uhlenhuth, it does not seem difficult to obtain strong antiserum, and all the tests tabulated were made with serums that would cause precipitates in lens dilutions of at least 1 : 5,000 and often much higher. The injection of rabbits with solutions of rabbit lens, however, does not seem to have the same antigenic effect—"Horror autotoxicus"—as the injection of lens

of other species. Contradictory results are reported on this point, and further study is required.

The tests are made by the contact method and the results read after one hour at room temperature. The

LENS PRECIPITIN REACTIONS *

	Lens Antiserums				Serum Antiserums					
	Beef	Horse	Sheep	Swine	Beef	Horse	Sheep	Swine	Human	Normal Rabbit Serum
Beef lens	+	+	+	+	0	0	0	0	0	0
Chicken lens	+	+	+	+	0	0	0	0	0	0
Dog lens	+	+	+	+	0	0	0	0	0	0
Guinea-pig lens	+	+	+	+	0	0	0	0	0	0
Horse lens	+	+	+	+	0	0	0	0	0	0
Human lens	+	+	+	+	0	0	0	0	0	0
Monkey lens	+	+	+	+	0	0	0	0	0	0
Rabbit lens	+	+	+	+	0	0	0	0	0	0
Rat lens	+	+	+	+	0	0	0	0	0	0
Sheep lens	+	+	+	+	0	0	0	0	0	0
Swine lens	+	+	+	+	0	0	0	0	0	0
Beef aqueous	+	+	+	+	+	0	0	0	0	0
Dog aqueous	+	+	+	+	0	0	0	0	0	0
Human aqueous	+	+	+	+	0	0	0	0	+	0
Rabbit aqueous	+	+	+	+	0	0	0	0	0	0
Sheep aqueous	+	+	+	+	0	0	+	0	0	0
Swine aqueous	+	..	..	..	0	0	0	+	0	0
Beef vitreous	+	+	+	+	+	0	0	0	0	0
Dog vitreous	+	+	+	+	0	0	0	0	0	0
Human vitreous	+	0	+	+	0	0	0	0	+	0
Monkey vitreous	+	+	+	+	0	0	0	0	0	0
Rabbit vitreous	+	+	+	+	0	0	0	0	0	0
Rat vitreous	+	+	+	+	0	0	0	0	0	0
Sheep vitreous	+	+	+	+	+	0	+	0	0	0
Swine vitreous	+	+	+	+	0	0	0	+	0	0
Beef serum	0	0	0	0	+	±	+	0	0	0
Horse serum	0	0	0	0	±	+	0	0	0	0
Human serum	0	0	0	0	0	±	0	0	+	0
Monkey serum	0	0	0	0	0	0	0	0	±	0
Sheep serum	0	0	0	0	+	0	+	0	0	0
Swine serum	0	0	0	0	±	±	±	+	0	0
Rabbit serum	0	0	0	0	0	0	0	0	0	0

* All lens antiserums active in all lens dilutions of 1 : 5,000 at least. Serum antiserums active in homologous serum diluted from 1 : 4,000 to 1 : 12,000. In some cases these antiserums react with the serum of related species. +, strong reaction; ±, slight reaction; 0, no reaction.

accompanying table shows all the lens solutions used (beef, chicken, dog, guinea-pig, horse, human, monkey, rabbit, rat, sheep, swine) to react in the same way with beef, horse, sheep and swine lens antiserums; further, that none of these lens antiserums react with the blood serum of either the corresponding or any of

the other species represented, and, conversely, that no serum antiserum reacts with any lens solution. The organ-specificness of the lens holds good throughout. The lens does not appear to contain any species-specific antigens.

The aqueous and vitreous humors appear frequently to contain lens substance, because in most instances these fluids in low dilutions or full strength react with lens antiserums. Uhlenhuth mentions that he obtained faint reaction with the vitreous and lens antiserum, but says nothing about the aqueous. These humors may react with serum antiserum also—not always—and then the law of species-specificness obtains. It is, of course, possible that in some of my specimens lens substance may have become mixed with either humor as a result of the handling incidental to the withdrawal of the humor; but I believe that in most instances this did not occur, as the withdrawal was made with special care to avoid undue pressure or suction.

The presence of lens substance in the vitreous and acqueous humors raises interesting questions in regard to the relations of these humors to the lens. Is the lens substance in the humors derived from the lens or on the way to be incorporated into the lens? If the last part of the question is answered affirmatively, what is the source of the lens material?

In the absorption experiments so far made the solution of any lens of those used in immunizing the rabbits removes all the precipitins from any of the lens antiserums mentioned, but here also further work is desirable. I may mention, too, that the serum of rabbits injected with extract of beef cornea reacts with beef serum, beef vitreous and beef aqueous, but not at all with beef lens or any other lens, indicating that the cornea contains species-specific proteins only.

SUMMARY

The precipitin reactions of the lens of certain mammals (and of the chicken) are lens-specific and the lens, at least of the mammals in question, does not appear to contain any species-specific precipitinogens; hence the lens protein may be regarded as chemically distinct

and as identical in diverse species. Perhaps further studies by means of lens-specific reactions may prove of interest.

April 11, 1921.

DIPHTHERIA AND DIPHTHEROID BACILLI OF THE ADENOIDS

I. PILOT

From the Department of Pathology and Bacteriology, University of Illinois, College of Medicine, Chicago

In order to determine the frequency of diphtheria and diphtheroid bacilli in the nasopharynx a bacteriologic study of extirpated adenoids was undertaken and the flora of the crypts of the faucial tonsils of the same individuals studied for comparison. The patients were children from 5 to 15 years of age without temperature elevation or any acute inflammatory condition of the throat or respiratory passages. The results of the cultures made on Loeffler's medium of the excised adenoids and tonsils are indicated in the following summary.

The adenoids of 100 children revealed B. diphtheriae in 12 per cent.

The crypts of the faucial tonsils of the same individuals harbored diphtheria bacilli in 12 per cent. When present in the tonsils the bacilli also occurred in the adenoids of the same person.

In the tonsillar crypts the diphtheria bacilli were usually more numerous than in the adenoids.

Two of the twelve strains were virulent; one showed attenuated virulence; three were pathogenic in large doses of the first culture while subsequent cultures were without virulence; the remainder were totally avirulent.

The diphtheroids occurred in 30 per cent of the adenoids and in 17 per cent. of the tonsils; when present in both they were decidedly more numerous in the nasopharyngeal vegetations than in the tonsillar crypts.

April 11, 1921.

ANEURYSM OF THE INTERVENTRICULAR SEPTUM OF THE HEART WITH HEART BLOCK

A. H. PEMBER AND FRED H. STANGL

From the Laboratory of Cook County Hospital

The patient was a negro laborer, 23 years old, who entered the Cook County Hospital March 24, 1921, complaining of shortness of breath, pain in the lower anterior chest and palpitation of the heart. These complaints dated back two years, but until two months before admission did not interfere with his usual daily work He also noticed that he was "out of breath" after climbing stairs, and during the night was obliged to sit up in bed to get his breath. The pain in the lower anterior chest was dull aching in character, not referred or affected by posture, but made worse by taking a deep breath. The palpitation had only been present for one month prior to entrance into the hospital. The patient stated that when he walked a short distance he "felt his heart pound."

Past History.—Chills and fever (malaria?) five years ago. "Rheumatism" three years ago affecting chiefly the left knee and both ankles. A sore on penis five years ago with no definite history of secondaries.

Family History.—Married four years, wife living and well and never has been pregnant. Mother dead, age and cause unknown. Father and three brothers living and well. One brother ill with rheumatism.

Personal History.—Never has used alcohol or tobacco to excess. General and Negative: Slept poorly, had occasional frontal headaches, appetite was good, no night sweats, slight weight loss, exact amount not known. No gastric disturbances, no hemoptysis, coughed at times, unproductive, no dysuria, polyuria, but for the last month urination has been D 6/N 3. At no time during life had the patient noticed any swelling of the ankles, abdomen, scrotum, hands or face.

Physical Examination.—Upon entrance, a well nourished, well developed adult male negro, 23 years of age, who did not appear acutely ill. The rectal temperature was 100 F. The radial pulse was 72 per minute, and the respirations were 24 per minute.

Head.—Scalp, eyes, nose, negative.

Eyes.—The pupils were equal, reacting to light and accommodation, no squint, no ptosis, no strabismus.

Buccal Cavity.—The teeth were in fair condition, needed cleaning, there were a few carious snags.

Tonsils were small. *Neck.*—The submaxillary lymph glands were palpable but small and hard. There was a visible pulsation in the left side of the neck, the rate of which was 100 per minute.

The chest was symmetrical and its expansion good. The excursion of the lungs was equal, fremitus and breath sounds normal throughout. The apical pulsation of the heart was diffuse and heaving in the fifth interspace at the mammary line and the rate was 72 per minute on admission. The heart rhythm was regular. The upper heart border was at the third rib; the right heart border at the right sternal margin, and the left heart border was 1 cm. outside the left mammary line. The total width was 14 cm.

By auscultation the first tone at the mitral area was replaced by a blowing murmur which was not transmitted into the left axilla or into the carotid arteries. The second pulmonic sound was accentuated.

The brachial blood pressure was 120 systolic and 80 diastolic. There was no pulse deficit.

The abdomen was flat, was not rigid, and no organs were palpable. No tumor masses nor tender points were demonstrable. The left testicle was about three times the size of the right.

Rectal examination revealed only external hemorrhoids.

Extremities.—No edema, no scars, no atrophy.

Reflexes	Right	Left
Eye (light and accommodation)	Pos.	Pos.
Tricepts	Pos.	Pos.
Abdominal	Pos.	Pos.
Cremasteric	Pos.	Pos.
Patellar	Pos.	Pos.
Achilles	Pos.	Pos.
Babinski	Neg.	Neg.

Urine normal.

Blood.—White blood count was 8,055. Blood cultures remained sterile. Blood Wassermann was positive.

The diagnosis of mitral regurgitation was made upon entrance. The patient was placed at rest in bed and no medication given. He gradually became worse, complaining continually of severe pain in precordium, for which morphin was administered.

On April 1, 1921, the jugular pulse was 100, the radial 40-50, indicating the patient had developed a heart block. On April 2, 1921, the patient suddenly became very cyanotic and showed signs of pulmonary edema. The systolic murmur was more marked than at previous examinations, being heard over the entire precordium and not transmitted. There was 1 cm. increase in the cardiac dullness, no edema of the extremities. The urine remained negative. The presence of above findings, positive Wassermann reaction on the blood serum led us to believe there might be luetic involvement of the Bundle of His.

The clinical findings remained the same until death, April 2, 1921, nine days after entrance into hospital. Permission was granted to examine the heart only at postmortem.

The heart weighed 590 gm. There was a saccular aneurysm of the ventricular septum 1½ cm. below the root of attachment of the aortic leaflet, projecting into the right ventricular cavity. The mouth of the aneurysm was 5 cm. from base to apex and 3 cm. wide. The lower margin of the mouth was 5 cm. from the apex of the heart. The greatest depth of the aneurysmal sac was 4.6 cm. The endocardium in the sac and about its orifice in the left ventricle was grey white and roughened from fibrous tissue. The wall of the aneurysmal sac was grey, firm, 4 to 5 mm. thick, and inelastic. From examination grossly the wall was apparently almost entirely fibrous.

In the right ventricle the tricuspid leaflets adjacent to the septum were firmly bound to the convexity of the aneurysm by fibrous adhesions. The posterior wall of the sac was closely fused with, and apparently a part of, the posterior ventricular wall, because the musculi pectinati were just in front of and against the sac. It was estimated that the sac had reduced the cavity of the right ventricle at least one half.

The mitral valve leaflets were smooth without any grossly demonstrable changes, the circumference of the valve ring was 12½ cm.

The aortic valves were thickened by white fibrous tissue and had on their margins of contact small mm. sized firm gray vegetative nodules. Except for a few small yellow fatty streaks, the intima of the ascending aorta was free from sclerosis. The left ventricular wall averaged 14 mm. in thickness, the right being 4 to 5 mm. The foramen ovale was closed. There were no changes of the auricles or appendages.

The presence of the vegetations of the aortic valve leaflets and positive Wassermann reaction suggested two possible etiologic factors producing this aneurysm: syphilis, and

embolic coronary occlusion. The latter seemed the more probable because of absence of aortic syphilis.

On numerous surfaces of the septum of the heart a branch of the coronary artery containing an organized thrombus was demonstrated. Upon microscopic examination beginning canalization of the thrombus was noted.

May 9, 1921.

THE INFLUENCE OF HEREDITY IN DETERMINING TUMOR METASTASIS

STUDIES IN THE INCIDENCE AND INHERITABILITY OF SPONTANEOUS TUMORS IN MICE

MAUD SLYE

Metastasis in this stock is somewhat rare. In 29,000 autopsies, furnishing something over 4,000 primary spontaneous tumors, about 19 per cent. of these tumors have metastasized. The general testimony of those who have discussed metastasis at all seems to be that the occurrence and location of metastasis is partly a mechanical matter, and partly a striking specificity of localization of secondary growths. This specificity they make no attempt to explain.

Ewing, speaking of metastasis in human tumors, states that in highly vascular tissues like the lip, stomach and testicle, very small carcinoma may yield distant metastasis. But these very organs are some of the ones whose tumors rarely metastasize in this stock, and then only locally. For example, in our lip carcinoma none has metastasized; among the testicle tumors one metastasized locally; while among the stomach carcinoma three showed metastasis into regional lymph nodes only. And this in spite of the close resemblance of these tumors to human tumors in similar organs.

In this stock mammary gland tumors rarely metastasize into regional lymph glands—in marked contrast to the reports concerning human breast tumors. Indeed, in many cases in this stock mammary gland carcinoma and sarcoma can be seen growing up to the lymph

gland but not invading it. On the other hand, pulmonary metastases from mammary gland carcinoma and sarcoma are common in this stock.

These divergences in the metastasis behavior of tumors of similar type and in similar organs, require some explanation other than merely the mechanical tendency of certain types of tumor to metastasize in certain locations.

The matter of tumor metastasis in this stock has been under observation for ten years and the data here given are based on over 29,000 autopsies, among which every case of metastasis is known.

Briefly stated these results show conclusively (1) In any given strain the metastatic tumors tend to occur most frequently in exactly the same organs in which the primary tumors of that strain occur. For example, if a strain runs high in primary liver tumors, many secondary liver tumors also will be found in that strain. Again, if a strain yields large numbers of primary lung tumors, metastasis will tend to occur in the lungs from primary tumors in almost any location. A strain which runs high in primary kidney tumors runs high also in secondary kidney tumors, etc.

2. In certain strains there is a tendency for tumors to metastasize into certain organs; whereas, in other strains, tumors of the same type in the same organ, even where they are of older and of larger growth, fail to metastasize into these organs. For example, in certain strains, practically every carcinoma of the mammary gland metastasizes into the lungs. I have many strains showing 100 per cent. of such behavior in these tumors. On the other hand, in other cancer strains, exactly this same type of mammary gland carcinoma, even where of older and of larger growth, never metastasizes into the lungs. I have many strains showing 100 per cent. of this type of behavior. Indeed, ever where tumor emboli are formed in the lungs of mice in these nonlung tumor strains, the emboli fail to take hold in the lung and no lung tumor is formed. This is a definite proof that the lung here fails to yield to tumor even where the tumor cells are present.

Again, strains which never yield primary lung tumor never yield secondary lung tumor. Strain 164 is a

striking example of this, where one family yielded 36 mammary gland carcinomas and sarcomas without one case of lung metastasis. In this family also there was never one case of primary lung tumor.

3. Individuals with secondary tumors in any given organ seem just as potent as individuals with primary tumors of that organ to transmit (by heredity) primary tumors in that same organ. For example, female No 3 with a primary carcinima-sarcoma of the mammary gland and secondary sarcoma in the kidney, transmitted primary kidney tumors to the strains derived from her, one family showing as high as 37 per cent. of primary kidney tumor.

Again, individuals with secondary lung tumors seem just as potent as individuals with primary lung tumors to transmit (by heredity) primary tumors of the lung. For example, many strains derived from a female with a primary mammary gland carcinoma with metastasis in the lungs, mated with a male showing primary lung carcinoma (double lung-cancer parentage), show 100 per cent. primary lung carcinoma.

4. Etiologic meaning: The fact that both primary and secondary tumors of a given organ tend to occur in the same strains and fail to appear at all in other strains, indicates that *heredity is a strong factor in determining not only where the primary tumors shall occur but also where the secondary tumors shall occur.*

This fact apparently means that the thing which is transmitted in the heredity of cancer is the tendency of an organ to yield to cancer, whether the lesion is primary in that organ or whether cells from the primary growth lodge in that organ and form a secondary lesion. Moreover, in strains from which tumors of a certain organ have been eliminated by heredity, even where cells from the primary neoplasm lodge in such organ, they fail to take hold and do not form a secondary growth. From these facts it is therefore evident that not only primary neoplasms, but also secondary tumors are determined in their occurrence and their location by heredity.

May 9, 1921.

(The full deails of this work will be published in the *Journal of Cancer Research.*)

ANEURISM OF VERTEBRAL ARTERY

H. GIDEON WELLS

A review of the literature shows that large aneurisms of the vertebral artery capable of producing pressure symptoms are extremely rare, although miliary aneurisms with or without rupture and aneurisms up to the size of a pea are common. In this case there was a spherical aneurism measuring 34x30x35 mm., involving the left vertebral artery in the cerebellopontine juncture, compressing the sixth to ninth cranial nerves. The aneurism was completely filled with a mass of dark clotted blood. As there was a distinct grooving in the base of the skull, the aneurism had evidently been present for a long time. The subject was a colored man 54 years of age, with no anatomical evidence of syphilis, but a history of cranial trauma many years ago. He died from a hypostatic bronchopneumonia after having been unable to work for about four months because of vertigo and facial neuralgia. Unfortunately a thorough neurological examination had not been made.

May 9, 1921.

(The details of this case will be published elsewhere.)

TRANSACTIONS OF THE
CHICAGO PATHOLOGICAL SOCIETY

VOL. XI. MARCH 1, 1922. NO. 6

DISSECTING ANEURYSMS OF THE AORTA

REPORT OF CASES AND REVIEW OF THE LITERATURE

DEAN P. CROWELL

There have been reported about 273 dissecting aneurysms of the aorta. According to Peacock,[1] Mannoir, in 1802, first gave the name of dissecting aneurysm to this condition. Yates,[2] a century later, found that in only two of these cases [3] had the nature of the disease been recognized during life. In two others,[4] the diagnosis was aneurysm of the aorta.

In 35 per cent. of the reports that I have reviewed (215), in which the condition of the aortic lining was described, there was advanced sclerosis with ulceration and calcification; in 42 per cent., a marked or moderate amount of fatty change or fibrous plaques, and in 9 per cent. such patches were few. In about one third of the remaining 14 per cent., the aorta had a thin wall or dilated lumen or both; in sixteen the vessel was thought to be normal. The wide discrepancies in the descriptions do not admit of precise statements as to the usual condition of the wall at the point of rupture; but the accounts indicate that either because of a general thinning (atrophy) or localized

1. Peacock: Tr. Path. Soc. London, 1863, p. 87.
2. Yates: Wisconsin M. J. **2**: 418, 1903-1904.
3. Prescott: J. Boston M. Soc. **2**: 134, 1897. Swaine: Tr. Path. Soc. London **7**: 106, 1855.
4. Borger: Ztschr. f. klin. Med. **58**: 282, 1905. Wyss: Arch. d. Heilk. **10**: 490, 1869.

disease, a weak place is present where the blood escapes from the channel. There are a number of reports of rupture caused by bacterial embolism into the aortic wall.[5] Usually, when dissection of the wall has begun, death follows in a short time or abruptly. Among other factors, such as valvular disease of the heart, old age, chronic nephritis, and increased arterial tension, the last probably is the most important. As an unusual cause of increased blood pressure in the proximal part of the aorta, narrowing or complete obliteration (coarctation) at the isthmus has been reported.[6] Although most writers mention exertion at the time of the onset of symptoms, in only a few instances has the exertion been unusual. Generally, the attack has occurred with moderate exercise, such as walking. As regards the age, in 80 per cent. of the 215 reports examined, it was 40 years or more, the entire range being from 13 to 95 years. This form of aortic disease is 1.64 times more prevalent in men than in women. In fifty-two cases, the condition of the kidneys was commented on, and chronic nephritis was found in 66 per cent. of these.

Kelynack[7] divides dissecting aneurysms into three classes: first, those in which the blood remains in the dissected aortic wall; a second variety in which the blood is forced into the surrounding tissues or cavities, and finally, those in which the blood reenters the aorta or, as has been the case in some instances, the iliac or other branches. Occasionally (6 per cent.) the last two are combined. Only 13 per cent of the cases fall in the first class. Unless death results from local pressure, interference with the circulation or causes remotely related to the aneurysm, organization of the intramural thrombus (fifteen cases) usually results. Kelynack's second group includes most of the cases (61 per cent.), and the perforation of the outer wall of the aneurysm into the pericardial sac, with sudden

5. McCrae: J. Path. & Bacterial. **10**: 373, 1905.

6. Wise: Tr Med. and Phys. Soc. of Calcutta **8**: 384. Barker: Med.-Chir. Tr. (n. s.) **25**: 131, 1860. Legg: Tr. Path. Soc. London **29**: 65, 1878.

7. Kelynack: Edinburgh M. J. **4**: 162, 1898.

death as its result,[8] commonly occurs. Hematopericardium was the cause of death in 47 per cent. of the reports reviewed. There may be hemorrhage into the pleural cavities or more rarely into the peritoneal cavity. Rupture into the trachea was found by Hoffman.[9] Occasionally, the blood infiltrates the periaortic or retroperitoneal tissue.[10] In the third class are 20 per cent of these cases. Almost always, canalization takes place, and the lining of the new channel may be sclerosed, even when the intima of the aorta is smooth.[11] Striking examples of this class resemble double aortas.[12] The point of reentrance is usually a tear in

FREQUENCY OF INVOLVEMENT

Artery	Number of Cases
Ascending part	150
Transverse part	106
Descending part	103
Thoracic part	97
Abdominal part	84
Innominate	19
Right common carotid	5
Left common carotid	11
Right subclavian	1
Left subclavian	11
Celiac	4
Superior mesenteric	4
Inferior mesenteric	1
Right renal	4
Left renal	3
Right common iliac	24
Left common iliac	41
External iliac	8
Internal iliac	6
Femoral	2
Popliteal	1

the inner wall of the sac; but it may also be at the site of aneurysmal amputation of one of the aortic branches.[13] The blood may reenter the aorta in several places along the course of the aneurysm. Peacock[14] divides the progress of the disease into three stages: first, rupture of the internal coats of the aorta; second,

8. Broca (Bull. Soc. anat. de Par. 1852, p. 275), Hayden (Proc. Path. Soc. Dublin **5**: 1, 1871) and others.
9. Hoffman: Arch. f. klin. Med. **7**: 590, 1869.
10. Bahrdt: Arch. d. Heilk. **13**: 473, 1872. Boyd: Lancet, 1840-1841, p 611.
11. Busse: Deutsch. Arch. f. path. Anat. u. Phys. **183**: 440, 1906.
12. Williams: Tr. Path. Soc. Philadelphia **18**: 151, 1898. Bouillaud: Arch. gén. de méd. **15**: 248, 1847.
13. Lebert: Traité d'anatomie pathologique, 1857, p. 752. Freibich: Ueber einen Fall von Aneurysma, Diss., welches ohne Sympt. wenigsten einige Woch. bestand, Würzburg, 1867.
14. Peacock: Tr. Path. Soc. London **14**: 87, 1863.

dissection and possible rupture externally, and third, recanalization. According to this division, 86 per cent. of the cases reviewed end in the second stage, and 14 per cent. in the third stage. The origin of the aneurysm is almost always in the ascending portion or arch, usually just above the aortic cusps. In a few instances, there have been multiple tears in which the aneurysm arose. Rarely, the primary rupture is found in the other portions of the aorta. These tears in the intima are most often from 1 to 3 cm. long; but they may involve almost the entire circumference.[15] When they occur in the ascending portion of the aorta they are usually transverse. Chiari[16] found a huge flap reflected from the inner wall of the aorta at its beginning, closing the mouths of the large branches of the arch. The primary rupture is of the intima, and most, or all, of the layers of the media. The dissection takes place in the outer layers of the media or between the media and adventitia. The branches of the aorta may be similarly dissected or cut across at their origins so as to arise from the outer wall of the aneurysm. The intercostal arteries are commonly cut off, and external pressure is the usual cause of interference with circulation in the large branches. The frequency of involvement by dissection in the various parts of the aorta and its branches is shown in the accompanying table.

There are thirty-five cases reported in which the dissection involves practically the whole length of the aorta.

Very little attention has been paid to the interference with the circulation in the branches of the aorta, caused by the splitting of the walls at the places where such branches have their mouths; and it may be safely assumed that the failure to recognize dissecting aneurysms of the aorta during life is at least in part due to failure to appreciate the fact that symptoms of this condition may be produced by interference with the blood supply in these branches. Only a few of the reports examined refer to the amount of the circumference of the aorta dissected at different distances in

15. Stewart: J. Path. & Bacteriol. **18**: 116, 1913-1914.
16. Chiari: Verhandl. d. deutsch. path. Gesellsch., 1909, pp. 207-209.

its length or to the location of such circumferential splitting. The following reports, however, consider this matter rather carefully. Boestrum [17] gives measurements of the width of the dissection at four different levels in his report of aneurysms involving most of the length of the aorta. Yates [18] shows by a drawing the area dissected. MacCallum,[19] describing one case, presents an excellent drawing, giving an accurate idea of the amount of circumferential dissection, and in another he simply states that almost all the circumference was involved. Shede [20] says that in his case all but the region between the intercostals was involved. Adami [21] presents a drawing which gives some idea of the area dissected, and his descriptions contain one or two transverse measurements. In thirty-one other reports in which mention was made of the width of the aneurysm, actual measurements made at one or two different levels were found in those by Luttick,[22] Geisler,[23] Clark,[24] Peacock and Schneckenbach.[25] In seven instances, the entire circumference was involved; in the remaining nineteen, the approximate amount of circumference involved is mentioned. Peacock says, "Generally, the sac occupies one half to two thirds of the circumference of the artery; but occasionally, and especially when the separation is continued from the trunk to its branches, the whole circumference of the artery is separated so that the canal is found entirely surrounding the original vessel."

With rupture into the pericardial sac (47 per cent.), the onset consists of a sudden severe pain in the chest and collapse. Following this attack, the patient may or may not rally. If death does not follow in a few minutes, a partial recovery is made; but a feeling of weakness, pressure or pain in the chest or fear of

17. Boestrum: Deutsch. Arch. f. klin. Med. **42**: 1, 1887.
18. Yates: Wisconsin M. J. **2**: 418, 1903-1904.
19. MacCallum: Bull. Johns Hopkins Hosp. **20**: 9, 1909.
20. Shede: Virchows Arch. f. path. Anat. **192**: 52, 1908.
21. Adami: Montreal M. J. **24**: 945, 1895, 1896.
22. Luttick: Virchows Arch. f. path. Anat. **100**: 180, 1885.
23. Geisler: Arb. a. d. path. Inst. zu Berlin, 1906, 282.
24. Clark: New York M. J. **7**: 92, 1859.
25. Schneckenbach, G.: Ueber einen Fall von diss. Aneurysma der Aorta, München, 1907.

impending death usually remains. Then within a few hours or days, a second similar pain is followed by almost immediate cardiac and respiratory failure.

If, however, rupture occurs into a cavity, signs of a large hemorrhage replace those of cardiac failure, and death is not so abrupt. Death from a widespread dissection with no external rupture may be sudden, the patient not recovering from the primary shock and coma; or it may be a matter of days of gradually weakening heart action.

Cases in which there was paralysis which might have been due to the interference with the blood supply of the spinal cord are reported by Dickinson,[26] MacCallum,[27] Barhdt,[28] Todd [29] and in this contribution. In those of Dickenson and Barhdt, there was paraplegia; in that of MacCallum, paralysis of the bowel and softening of the brain, and in Todd's case, hemiplegia. In one of those here reported, there was hemiplegia, and in another, paralysis of one leg. There was also severe abdominal pain in Barhdt's case, and this symptom is ascribed to interference with the blood supply to the intestines, in cases reported by Thompson,[30] Adami,[31] Edwards and Stone,[31] Freundlich,[32] Mandron,[33] Bludau [34] and Kaiser.[35] In the last two, abdominal operations were performed because of the diagnosis of "surgical abdomen." In two cases in which the iliac arteries were involved, there was pain in the leg.[36] In four cases with interference of the subclavian circulation, there was pain in the arm.[37] In a case in which both iliacs were affected, Swaine [38] noticed absence of pulsation in the femorals, while

26. Dickenson: Tr. Path. Soc. London **13**: 48, 1862.
27 MacCallum: Footnote 19, Case 5.
28. Barhdt: Arch. d. Heilk. **13**: 473, 1872.
29. Todd: Tr. Med.-Chir. **17**: 301, 1844.
30. Thompson: Med. Gazz. London **37**: 584, 1846.
31. Edwards and Stone: Tr. Path. Soc., Philadelphia **6**: 38, 1878.
32. Freundlich: Zwei Fälle v. aneur. diss. aortae, Würzburg, 1893.
33. Mandron: Bull. Soc. Anat. **39**: 388, 1864.
34. Bludau: Ein Fall v. Aneur. diss. Aortae, Halle a. S., Dresden, 1909.
35. Kaiser: Ein Aneur. diss. der Brust und Bauchaorta als Ursache eines paralytischen dünndarm-Ileus, Berlin, 1913.
36. Oliver: Lancet **1**: 1068, 1892. Freundlich: Footnote 32.
37. Barker: Tr. Med.-Chir. n. e. **25**: 131, 1860. Leggat: Tr. Path. Soc., London **20**:-130, 1869. Hayden: Proc. Path. Soc., n. s., Dublin **5**: 1, 1871. Peabody: Med. Rec. **8**: 326, 1880.
38. Swaine: Tr. Path. Soc., London **7**: 106, 1855.

Draper [39] found loss of pulsation in the right radial artery in a case in which the innominate artery was plugged by a dissected flap from the ascending portion of the aorta. Flockman [40] states that in his case in which there was pressure at the origins of the large branches of the arch, death resulted in a manner similar to that occurring in dogs in which both carotids were tied off.

REPORT OF CASES

Case 1.—*History.*—H. P., man, aged 50, was taken to the Cook County Hospital by the police, May 23, 1918, after he had been removed in coma from a street car, with symptoms which led to the diagnosis of probable cerebral hemorrhage or uremia (service of Dr. Koessler). Examination revealed coma; respirations, 24, stertorous and of the Cheyne-Stokes type; deviation of the eyes to the right; flaccid paralysis of the legs and right arm; spastic paralysis of the left arm; irregular pulse of 62; systolic blood pressure, 105, diastolic, 65; systolic murmur heard at the apex; clear heart tones; moderate sclerosis of the radial arteries; slight edema of the right leg; vasomotor changes of the right leg and abdomen; albumin in the urine; leukocytosis of 29,500; temperature, 98.2 F. Five hundred cubic centimeters of Fischer's solution was given intravenously after the withdrawal of 100 c.c. of blood, and stimulants were administered; but he died in six hours.

Necropsy (Dr. E. R. LeCount).—This revealed: marked syphilitic sclerosis of the aorta, iliac, common carotid, subclavian, axillary, vertebral and cerebral arteries; huge dissecting aneurysm of the aorta and the innominate, common carotid and iliac arteries; compression of the channels of the common carotid arteries; miliary gummas of the liver; syphilitic scars of the leptomeninges; venesection wound of the right cubital fossa; anemia of the brain; edema of the brain and leptomeninges; foramen magnum pressure-furrow of the brain-stem; marked sclerosis of the coronary arteries; chronic diffuse nephritis, red, granular kidneys; marked hypertrophy of the left ventricle of the heart; clot-distended right heart chambers; marked edema of the lungs; enlarged superficial veins of the abdomen, thighs and legs; varix of the right spermatic vein; chronic purulent left frontal sinusitis, and disseminated focal atrophy of the cerebral cortex.

39. Draper: Med. Rec., 1866.
40 Flockman: München med. Wchnschr., 1898.

Fig. 1.—Conditions in Case 1: *A*, innominate artery; *B*, left common carotid artery; *C*, extent of splitting of the wall of the left subclavian artery; *D*, celiac axis; *E*, superior mesenteric artery; *F*, renal artery; *G*, midline of the aorta behind, and *H*, extent of the splitting of the wall of the left external iliac artery. This and the accompanying illustrations are from life-size charts drawn "to scale" and then reduced.

The dissecting aneurysm, starting in the edge of a plaque at the mouth of the right coronary artery where there was a transverse slit in the intima, 1 cm. long, ran in the right posterior portion involving one third of the circumference. As it reached the arch of the aorta, it narrowed to 2 cm. and came to lie on top of the vessel, passing to the left as it reached the descending portion. It involved the mouths of the innominate, left carotid and subclavian vessels, and from the arch, passed down to lie in the posterior half of the thoracic portion. Before reaching the abdominal portion, it curved again to involve more of the left side and then in the abdominal portion came to include more of the right side and less of the left. (Fig. 1[41]). At the mouth of the superior mesenteric artery, it was 3.5 cm. wide, at the bifurcation 2.5 cm. It dissected the back half of the wall of the left

Fig. 2

Fig. 3

Fig. 2 (Case 1).—Innominate artery: *A*, ulcers of the intima.
Fig. 3 (Case 1).—Left common carotid artery.

iliac artery for 5 cm. It also extended up both common carotid arteries to their bifurcations, involving the left half of the circumference in the left, the front left quarter in the right. Only about 1 sq. cm. of the wall of the left subclavian at its origin and a similar place of the left external iliac were involved. In that part of the aneurysm in the left carotid, there was an adherent thrombus completely filling it. The right subclavian artery was not involved. At the bifurcation of the innominate were two ulcers of the intima, each 5 mm. in diameter. The microscope showed syphilitic changes in the aorta and a dissection of some media with the adventitia to form the outer wall of the sac.

Case 2.—*History.*—L. T., a negress, aged 71, was taken to the Cook County Hospital after an illness of two days, with

41. The black regions in this chart, as in subsequent charts, indicate the location of the dissection of the aorta and its branches.

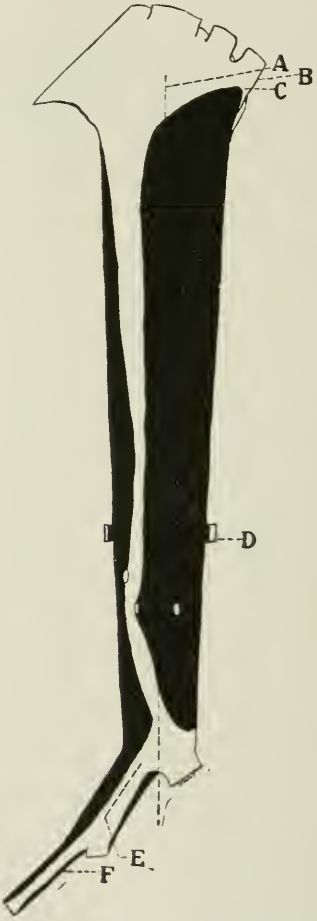

Fig. 4.—Conditions in Case 2: *A*, midline of the aorta behind; *B*, subclavian artery; *C*, rupture of intima; *D*, celiac axis; *E*, midline of right common iliac behind, and *F*, external iliac artery.

symptoms which led to the diagnosis of cerebrospinal syphilis (service of Dr. Grinker). Examination revealed shortness of breath, slight nausea and vomiting, pain in the abdomen, spastic paresis of the right leg, pulse 108, diastolic, and 131,

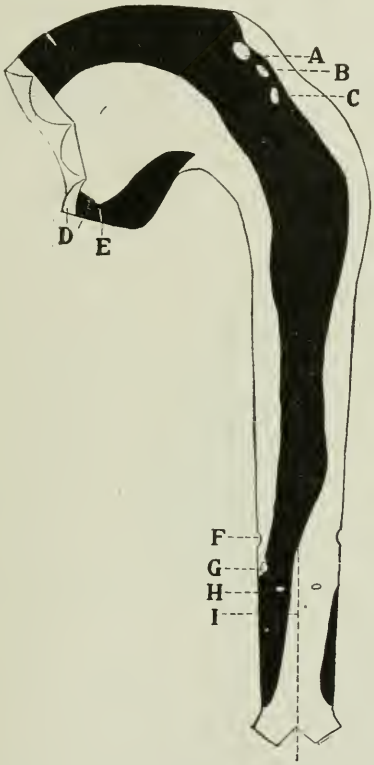

Fig. 5.—Conditions in Case 3: *A*, innominate artery; *B*, common carotid artery; *C*, subclavian artery; *D*, aneurysm; *E*, half of slit in intima; *F*, celiac axis; *G*, mesenteric artery; *H*, renal arteries, and *I*, midline of aorta behind.

systolic, and a history of chronic headaches and sudden coma of two hours' duration on the day preceding admission. Two weeks after admission, there was profuse bleeding from the bowel, lasting two days, after which she gradually weakened and died, twenty-three days after the onset of her illness.

Necropsy (E. R. LeCount).—This disclosed: marked generalized senile arteriosclerosis; huge dissecting aneurysm of the thoracic and abdominal portions of the aorta, left common and external iliac artery; aneurysmal dissection of the beginnings of the celiac axis, left renal and superior mesenteric arteries; fusiform aneurysm of the celiac axis; aneurysmal amputation of the inferior mesenteric artery in the aortic wall; partial pressure occlusion of the mouths of the left common carotid and subclavian arteries by mural aortic thrombi; mural thrombosis of the aorta, celiac axis and left middle cerebral artery; extensive spontaneous hemorrhage into the retroperitoneal tissues, beneath the peritoneum of the mesentery, lesser omental cavity and small pelvis; anemia of the brain; edema of the leptomeninges; clot-distended heart chambers and large blood vessels; hypostatic hyperemia of the lungs; moderate generalized icterus; disseminated atrophy of the cerebral cortex; chronic diffuse nephritis and arteriosclerotic kidneys.

The aneurysm, starting at the distal margin of the mouth of the left subclavian artery in a slit 5 by 1 mm., involved the posterior three fourths of the thoracic portion, the posterior four fifths of the abdominal portion, the front half of the right common iliac and 6 cm. of the front half of the external iliac. The proximal 1 cm. of the celiac axis was entirely involved, and the adjacent 2 cm. to a lesser extent. The proximal 1 cm. of the left renal and superior mesenteric artery was similarly affected. The inside of the aneurysm was rough, irregular and nodular from fibrin deposits which had undergone organization. Along the entire aorta, but less in the proximal 10 cm., there were marked sclerotic changes and many lime deposits. Grossly, the splitting had occurred between the media and adventitia.

Case 3.—*History.*—A teamster, aged 61, was taken to the Cook County Hospital with symptoms which led to the diagnosis of epilepsy and pneumonia (service of Dr. Hall). Examination revealed irrationality, stupor, impaired resonance over the right lower lobe, blood-stained sputum, temperature of 102 F., increased area of cardiac dulness and loud systolic murmur at the apex. Preceding death, which occurred in thirty-six hours, there were left hemiplegia, involuntary urination and defecation and Cheyne-Stokes respiration.

Necropsy (E. R. LeCount).—This revealed: syphilitic and senile sclerosis of the aorta, dissecting aneurysm of the entire aorta and rupture of this aneurysm into the pericardium; hemopericardium; fibrous pleuritis, and partial atelectasis of the right lung.

The aneurysm, starting in a transverse slit, 2.1 cm. long, and 2 cm. above the aortic cusps, involved about a third of the circumference of the ascending portion and almost two thirds of the remaining portions. It involved the posterior half more than the anterior, and cut off most of the intercostal and lumbar vessels at their origins, but none of the large branches, and ended at the bifurcation. The dissection also extended back to the intrapericardial portion of the aorta, where the rupture into the pericardium occurred. There were marked changes in the intima of the entire aorta, least in the proximal 10 cm. and distal half. The roughen-

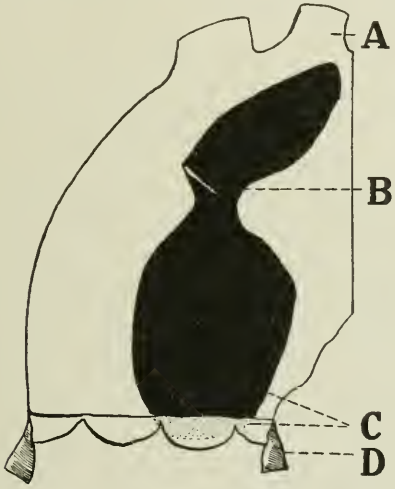

Fig. 6.—Conditions in Case 4: *A*, common carotid artery; *B*, slit in intima; *C*, dissected region, and *D*, heart wall.

ing in the ascending portion and arch was typical of syphilis, and elsewhere there were many ulcers and calcareous plaques. The dissection where examined microscopically was in the outer edge of the media.

Case 4.—*History.*—N. H., a woman, aged 60, entered the Cook County Hospital, Jan. 2, 1902, and died the same day. No further clinical history was obtainable.

Necropsy (Dr. W. H. Hunter).—Only the heart and aorta were described. The wall of the left ventricle was 2 cm. thick, the endocardium negative. The aortic cusps were slightly thickened and stiffened by small calcareous plaques. The pericardium was filled with partially clotted blood. Hematopericardium was stated as the cause of death.

The dissecting aneurysm, starting in a transverse slit through the intima and media, 2 cm. long, 4 cm. above the valve attachments, extended in both directions to take somewhat the shape of a canoe paddle. The splitting was up as far as the origin of the subclavian artery and proximally so as to involve about 1 cm. of the base of the heart where a rupture into the pericardium had taken place. Grossly, the dissection was between the media and adventitia. At the site of rupture of the intima were several atheromatous nodules, while the entire arch and descending portion of the aorta were the seat of marked sclerosis, in many places cartilage-like in firmness.

December 13, 1920.

REPORT OF A CASE OF MEGACOLON IN AN ADULT

WILLIAM C. BUCHBINDER

From the Pathology Laboratories of the Cook County Hospital

Megacolon in adults is a sufficiently rare condition to warrant the placing on record of this isolated case.

This patient, a white male, 50 years old, a plasterer by occupation, was admitted to the Cook County Hospital, service of Dr. J. L. Miller, July 16, 1921. He complained of shortness of breath, pain in the legs, varicosed veins of the legs, swelling of the scrotum, blood in the stools, and diarrhea. The shortness of breath had been noted for five or six years; the diarrhea had been present for six months and the passages more than twenty per day of a watery character, and streaked with blood and pus.

Blood in the stools had been noted for the same period as the diarrhea, and occasionally large clumps of clotted blood were passed.

There was no history of obstipation at any time. Other points in the history to be noted were the heavy consumption of alcohol for many years; typhoid fever twenty-five years ago; and a history fifteen years previously of having weighed 400 pounds. Physical examination revealed a well developed moderately obese adult white male, weighing about 200 pounds and apparently about 50 years of age. There was moderate cardiac enlargements to the left. There were no abnormal sounds. The abdomen was moderately distended, and an ascites was determined on percussion. No rigidity

was ever noted but tympanitis was demonstrated. Varices were present about the umbilicus, and there was a reducible umbilical hernia. Edema of the scrotum was marked, and there was beginning ulceration. The lower extremities were markedly edematous. The urine was alkaline; there were epithelial and pus cells, and a two plus albuminuria. There were 3,200,000 red blood cells per c.mm. of blood; 9-12,000 white cells (60 per cent. polymorphonuclear leukocytes). The blood showed an increase in urea and urea nitrogen. His blood pressure was: systolic, 110; diastolic, 55. Blood was detected macroscopically and chemically in the stools.

The clinical diagnosis was: Myocardial degeneration with loss of compensation; passive congestion of the liver (or portal cirrhosis?) obesity; umbilical hernia.

The diarrhea became intractible and the abdominal pain severe several weeks after entrance, and carcinoma of the bowel was suspected. The patient was very difficult to control, and further diagnostic methods could not be well instituted. No roentgen ray of the intestines was made. The patient refused treatment and was discharged about six weeks after admission.

On September 21, about three weeks after his discharge, the patient was readmitted to the hospital as an emergency attempted suicide with lacerations of the right arm. A thorough physical examination was not made and the patient died six hours after entrance. Marked distension, however, of his abdomen was noted.

At the necropsy (Dr. W. B. Moody) the colon was enormously enlarged and distended with gas, containing a moderate amount of yellow pasty feces. There was about 150 c.c. of a faeculent material in the abdominal cavity. There was a spontaneous perforation of the sigmoid at the site of a large annular ulcer, the perforation occurred shortly before death, or postmortem, as there was no peritoneal reaction. Other findings were moderate hypertrophy of the heart; marked increase of epicardial fat; moderate patchy sclerosis of the coronary arteries. The empty colon taken from the body weighed 2,030 g. It was 221 cm. long. Its walls were everywhere greatly thickened except at the ascending portion where there was a moderate hypertrophy, the white line being present there, but the sacculations absent, and its lining smooth and glistening.

The cecum was thickened to .5; the sigmoid to .7; and the rectum to 0.8 cm. The circumference of the cecum was 35; the ascending portion 18; the transverse colon 21; the sigmoid 24.5, and the rectum 21.5 cm. The appendices epiploicae were large and up to 2.5 cm. in diameter. The mesentery

was thickened to .8 cm. There was an annular ulcer 9 cm. wide, 22 cm. above the anus. On the proximal side of the ulcer for 10 cm. there were numerous circular shallow ulcers having the greatest diameter of .5 cm., there being about 2 to the square cm. The floors of the ulcers were smooth and consisted of muscularis.

Histological section of the huge annular ulcer did not reveal evidence of malignancy.

COMMENT

The history presented is atypical in that coprastasis, ordinarily prominent in these cases, could not be elicited at any time. The diarrhea, abdominal cramps, and bloody stools could be attributed to the marked ulcerative process of the sigmoid. The marked hypertrophy and dilatation of the sigmoid and rectum below the possible point of obstructions allows of classifying the specimen as a true megacolon as opposed to the acquired or pseudo megacolon. Marked dilatation if the large intestine in cases of slow cardiac death, such as this, may be due to gas producing organisms.

October 10, 1921.

INHIBITORY ACTION ON TUBERCLE BACILLI OF SOME NEW MERCURY COMPOUNDS

LYDIA M. DEWITT

Otho S. A. Sprague Memorial Institute and the Department of Pathology, University of Chicago

A number of organic mercury compounds of phenols and of anilines have been tested for their comparative efficiency in inhibiting the growth of human tubercle bacilli in glycerol agar. The results may be summarized as follows:

1. The power of phenol to inhibit the growth of the tubercle bacillus is greatly increased by the substitution of a mercury salt in place of one of the hydrogens (thus a mercury atom attached by one bond to carbon).

2. It is also increased by the substitution of one NO_2 for a hydrogen, the degree of increase of inhibitory power varying with the position of the NO_2 group, the ortho position being most favorable, para next and the meta least.

3. The position of the mercury group also has much influence on the degree of increase of inhibitory power, the ortho position again seeming most favorable.

4. The mercury bridge compounds, at least the two tested ones, in which the bridge was in the ortho position also have a high inhibitory power.

5. Saligenin or phenol O-carbinol has the same inhibitory power as phenol, but its mercury compounds have a much greater power while the nitro mercury saligenin has a much greater inhibitory power than the simple mercury saligenin.

6. In the anilin compounds also, the substitution of a mercury soluble salt or of a nitro group, or of both greatly increased the inhibitory power of the anilin.

7. Methyl and ethyl groups do not apparently affect the antiseptic power of these compounds although those mercury compounds of anilin having methyl or ethyl groups and nitro groups substituted have a very high inhibitory power, not apparently varying very much with the per cent. of mercury or with the relative position of the other groups.

October 10, 1921.

A METHOD OF RECORDING SPECIMENS IN THEIR FRESH STATE BY MEANS OF STEREOSCOPIC "LUMIERE" PHOTOGRAPHS

EMIL G. BECK

It is indeed regrettable that there are not preserving fluids which will retain the natural colors of pathological specimens.

In visiting a Pathological Institute and examining a collection of rare specimens, one is impressed with the change of appearance of the specimens which they had at the time they were removed from the body. Just

imagine if all of these specimens had retained the natural color which they had in their fresh state, what a wonderful exhibit they would furnish.

For the past 12 years I have adopted a method which I think will come nearest to my ideal of preserving for record the appearance of specimens as they actually were at the time of the operation.

The method consists in taking *stercoscopic* photographs on "Lumiere" plates as quickly as possible after their removal from the body of the specimen before any changes have taken place, and the gloss or shining membranes are still present.

I desire to present to this Society tonight a series of plates illustrating this method. From my collection which I have accumulated during the past 12 years, I have selected about 25 plates of various types of specimens. It is very difficult to describe the appearance of these specimens on these glass plates; but a single glance at any one of these plates will convince the observer of the usefulness of this method.

The colors are reproduced (if the picture is taken by an expert), so true to nature that even in the single picture will be given an excellent likeness of the specimens; but the stereoscopic picture gives more. It gives a lifelike picture so that one may think of inspecting a fresh specimen.

It is possible to reproduce these colors on a card by a four colored process which I developed some 9 years ago and published with illustrations in "Surgery, Gynecology and Obstetrics." It is impossible, however, to make the reproduction quite as perfect as the glass plate itself; but it is nearer to the true color than any of the artificial color drawings that I have ever seen in textbooks or publications.

The only objection to this method is the cost of production, although it is not prohibitive. Each plate including the photographer's fee does not exceed $2, and reproduction on paper is more expensive than that of the ordinary black print. Inasmuch as it has to go through the press 4 times, it must be thoroughly registered.

November 14, 1921.

CHANGES IN THE REACTION OF THE BLOOD DURING ANAPHYLACTIC SHOCK *

EDWIN F. HIRSCH
AND
J. LISLE WILLIAMS

From the Pathological Laboratory of St. Luke's Hospital, Chicago

There seems to be no mention in the literature of changes in the H-ion concentration of the blood during anaphylactic shock. Recently Eggstein [1] reported a lowering of the alkaline reserve, apparently in proportion with the severity of the shock. Rabbits were sensitized by intraperitoneal injections of the proteins and the H-ion concentration of the blood was determined by the gas chain method. In all of these experiments there is a diminished alkalinity of the blood during anaphylactic shock, as well as a lowering of the alkaline reserve as Eggstein reported.

November 14, 1921.

THE EFFECT OF THE MODE OF DEATH ON LUNG CHANGES IN RABBITS AND GUINEA-PIGS

SARA E. BRANHAM

From the Department of Hygiene and Bacteriology, the University of Chicago

Every now and then in medical literature, and especially in reports of research involving experiments with animals, one finds reference to peculiar hemorrhagic lung lesions. Occasionally considerable significance has been attached to these and they have been interpreted in direct relation to the experiments in which they have been found.

* A complete report will be published in *The Journal of Infectious Diseases.*

1. Jour. Lab. and Clin. Med. (1921) 6, p. 555.

Aufrecht, in his studies on the nature of colds, reported experiments on rabbits which he exposed to severe chilling for varying lengths of time. When these were killed marked hemorrhages were found both in the interstitial tissues of the lungs and into the alveoli. These he interpreted as a result of the chilling on the animals. His rabbits were killed by a blow on the back of the neck.

More recently at least five different groups of men have reported similar hemorrhagic lesions in animals which were inoculated with influenza material. The animals used included rabbits, guinea-pigs, and mice. In some instances the manner of killing them is not given, but in those cases where the method is stated they were killed by a blow on the back of the neck.

Similar hemorrhagic lesions have been described, but with less satisfactory detail, in animals inoculated with material from cases of lethargic encephalitis and nephritis.

In some of these reports details concerning these hemorrhages are lacking, but where descriptions have been given there seems to have been a marked uniformity in the pathological picture, both macroscopically and microscopically.

A careful search of the literature pertaining to experimental medicine would perhaps yield many other instances in which such hemorrhages have been noticed and in which considerable importance has been attached to them.

During this last year we have found striking hemorrhagic lesions in the lungs of a large number of rabbits and guinea-pigs. Of 46 animals that have been killed in the course of some experiments that we have had under way, 24, approximately one-half, have shown them to a marked degree. These lesions seem to have been strikingly similar to those referred to above. The most outstanding features were: (1) That the lungs did not usually collapse when the thorax was opened, but remained quite large in volume. (2) The lungs were more or less mottled by bright red areas of hemorrhage, sometimes diffuse and sometimes patchy, varying in size from a mere pinhead to several

square centimeters, and sometimes entirely involving a lobe. These were not superficial, but extended into the deeper portions of the lung. The bright red color gave the impression that these hemorrhages were very fresh. Occasionally darker and more purplish hemorrhages accompanied the brighter ones. There was no consolidation nor congestion anywhere.

Sections for microscopic study showed a marked emphysema. There was hemorrhage into the alveoli, and in the most severe cases into the bronchi. In some only about 5-10 per cent. of the alveoli contained blood; in others 50-70 per cent. There was no real leukocyte reaction.

Both emphysema and presence of similar hemorrhages have been found in anaphylaxis. There was no possible anaphylaxis here. Most of the animals in which these lesions were found were healthy young rabbits and guinea-pigs just from the breeding farms, which had never been used in any previous experiment.

The first 6 rabbits were killed by a blow on the back of the neck. The animals were held by the hind legs, with the head down, and the blow directed in such a way that the skull was not at all injured. Only one of these rabbits showed the hemorrhagic areas. These were very small but quite abundant.

The next 13 rabbits were held by the ears with the head up, the same care being taken not to injure the skull. This change in the position of the animal was made purely as a matter of convenience, and was not planned. Of these 13 rabbits, 13, or 100 per cent., showed abundant and striking lung hemorrhage.

This result made it seem that either the animals in this second series were the victims of a peculiar epidemic, or else that the way in which they were killed was a factor in the production of the lesions. Therefore it was decided to kill the next series by ether. Five were anesthetized and the chest opened while the animals were still alive. The lungs of all 5 were well collapsed and quite normal in appearance. Sections of some of these showed atelectasis, no hemorrhage, and no evidence of any pathological change.

After this some animals were killed by each method. All of the guinea pigs were either held by the feet or etherized. It was inconvenient to hold them by the ears. The results may be summarized as follows: 46 animals have been killed since these observations were begun—39 rabbits and 7 guinea-pigs. Of the 39 rabbits, 8 were held by the feet with the head down. Only 1 showed uncollapsed hemorrhagic lungs. Of 23 held by the ears with the head up, 20, or 87 per cent., had abundant and striking hemorrhage, while only 3 did not. Of 8 killed by ether, none showed hemorrhage; all had lungs well collapsed and of a normal grayish pink color. Of the 7 guinea-pigs, 6 were held by the hind feet and killed by a blow on the back of the neck. Four were positive and 2 negative. The lungs of the one guinea-pig killed by ether were normal.

The weight of evidence in the 46 cases cited above in favor of a relation between these hemorrhagic lesions and a blow on the neck was purely circumstantial. Attempts to observe the effects of first ether and then a blow on the same animal were made with 4 rabbits. Each animal was anesthetized and a cannula put into the trachea so that artificial respiration could be applied. The chest cavity was opened and the lungs examined in situ. While artificial respiration was continued the animal was held up by the ears and given a sharp blow on the back of the neck. Then the lungs were removed and reexamined. The results were not conclusive. In each of the 4 rabbits the lungs after the ether only appeared free from hemorrhage and normal. After the blow there were a few small bright red pinhead hemorrhages scattered here and there, but no more than might easily have been overlooked when the lungs were examined in situ.

This report is essentially a confirmation of the findings of Maitland, Cowan, and Detweiler at the University of Toronto, and of Foord in work done in the Department of Pathology at the University of Chicago. The first three, working together, found lesions apparently identical, macroscopically and microscopically, with those just described in approximately one half of a large number of animals. Their animals were killed

either by a blow on the back of the neck, the position in which they were held not being stated, or by chloroform. Foord, in repeating the experiments of Aufrecht on the effect of chilling on rabbits, found hemorrhages in as many unchilled animals as chilled when they were killed by a blow on the neck. He found them abundantly in one animal killed with KCN, but very few in those killed with chloral. The conclusion reached by all of these investigators was that these hemorrhages were an agonal phenomenon.

These hemorrhages have not been constantly found in animals killed by a blow on the back of the neck. They have been reported in some killed in other ways, as, for example, in the rabbit killed with KCN by Foord. But finding them in 67 per cent. of all animals killed by a blow on the neck and in 87 per cent. of those which were held head up when the blow was given, seemed to indicate that the mode of death had something to do with their occurrence.

I shall not attempt to offer any explanation of these lesions. I only wish to emphasize the fact that these hemorrhages do occur with considerable frequency in apparently normal rabbits and guinea-pigs under certain conditions, and that this should be borne in mind in using these animals for experimental purposes.

(A more complete account of this work will be published elsewhere.)

December 12, 1921.

POST-TRAUMATIC CALCIFICATION OF THE PANCREAS, WITH DIABETES

H. GIDEON WELLS

A previously healthy young man fell from a wagon and was probably run over by at least one of the wheels. He received fractures of several ribs on the left side, traumatic infarction of the left adrenal, the upper pole of the spleen, and the entire left kidney, together with a crushing injury of the pancreas which resulted in almost complete destruction of the secreting

elements, which were replaced by a large quantity of dense fibrous tissue and extensive deposits of calcium salts. Analysis showed that about 64 per cent. of the dry weight of the pancreas consisted of inorganic salts, chiefly calcium carbonate. Jacksonian epilepsy developed, the result of necrosis of a considerable area of the cerebral cortex, presumably occurring at the same time as the other injuries. The patient became rapidly emaciated, exhibited great thirst, and the urine found in the bladder at autopsy contained sugar. A review of the literature has failed to reveal a similar case of extensive pancreatic calcification, whether post traumatic or otherwise, or an analogous case of diabetes following crushing injury of the pancreas.

The full details of this case will appear in the *American Journal of Medical Sciences*.

December 12, 1921.

BLOOD CHANGES IN EXPERIMENTAL TUBERCULOSIS

LAURETTA BENDER
AND
LYDIA M. DEWITT

This work was begun with the idea of obtaining another method besides the duration of life, weight curves, and postmortem findings by which Dr. DeWitt might judge the results of her chemotherapeutic work in experimental tuberculosis in guinea-pigs. The study is not yet completed, and this report covers only part of the work done on untreated animals, although we are now beginning to apply it to the treated animals.

The guinea-pigs were inoculated with a human strain of tubercle bacilli. The usual clinical methods have been applied in obtaining blood from the ear and examining it for the number of erythrocytes and leukocytes, the percentage of hemoglobin (Sahli method) and for the differential count of leukocytes. Examinations have been made once a week of all but the uninoculated controls, which were examined once in two weeks.

The counts of the uninoculated or normal guinea-pigs made relatively smooth curves, except where acute infections have developed. Then the usual polymorphonuclear leukocytosis resulted and, in severe cases, an anemia with a decrease in erythrocytes and hemoglobin and an appearance of nucleated erythrocytes. Otherwise a normal average may be estimated as follows:

Erythrocytes	6,000,000
Hemoglobin	95%
Leukocytes	10,000 to 15,000
Lymphocytes	35% to 55%
Large Mononuclears	3% to 7%
Transitionals	1% to 3%
Neutrophils	35% to 60%
Eosinophils	3% to 4%
Basophils	1%

A chronic infection developed in animals which received relatively light inoculations and showed a prolonged resistance to the disease, living nine months or more after inoculation. The curves of these animals all show marked irregularities as compared with those of the normal animals.

The erythrocytes varied between 5,200,000 and 6,500,000. In the early stages they frequently exceeded the normal. The hemoglobin followed the curve of the erythrocytes, but decreased relatively more rapidly. It varied between 65 per cent. and 97 per cent. In no instance were nucleated erythrocytes noted.

The leukocytes varied between 10,000 and 20,000. Leukocytosis was always due to the polymorphonuclear cells. No true lymphocytosis of any marked degree was ever noted. There was a marked eosinophilia of from 5 per cent. to 30 per cent. appearing from five to ten months after inoculation and disappearing previous to death, if death was due to tuberculosis. There were no variations in the large mononuclears, transitionals or basophils.

An acute infection was developed in animals that were heavily inoculated. They usually died of a generalized tuberculosis in less than four months.

There was a rapid fall in erythrocytes sometimes reaching as low as 3,500,000 at time of death. The

hemoglobin dropped more rapidly than the erythrocytes, occasionally to 35 per cent. Nucleated erythrocytes were noted in only two cases and then did not exceed two to every 100 leukocytes.

The leukocytes varied between 4,000 and 25,000. The leukopenia was more marked than the leukocytosis. Where leukocytosis occurred it was always due to the neutrophil polymorphonuclear cells.

The lymphocytes showed a steady decline until at the time of death they were frequently only 10 per cent. or less of the total leukocytes.

The large mononuclears and transitionals usually showed an increase to double or more their usual number, ten days or two weeks previous to death. At time of death, they sometimes each exceeded the number of lymphocytes, or they may be themselves again decreased.

Eosinophils were decreased or absent in all but one case. This animal had an eosinophilia of from 4 per cent. to 7 per cent.and lived four and one-half months, which was a longer duration of life than that of any other acute case.

January 9, 1922.

THE FUNCTION OF COLOSTRUM

H. GIDEON WELLS
AND
JULIAN H. LEWIS

Summary.—The blood of new-born infants, and probably of all other mammals, contains little or none of the serum protein or protein fraction known as the euglobulin. This seems to be supplied chiefly by the colostrum, which differs from milk in containing a large amount of this protein secreted directly from the blood. The euglobulin is the only blood protein that appears in the colostrum, and it is the only protein fraction in which the new-born infants' blood is deficient. Evidently the colostrum is formed to provide the fetus with a supply of euglobulin for its blood,

during the short period immediately after birth when proteins may be best absorbed without disintegration by digestive proteolysis. The importance of this lies in the fact that the protective antibodies of the blood are found associated with the euglobulin fraction, and that the quantity of protective antibodies found in the colostrum, the milk and the infants' blood varies directly with the euglobulin content of these fluids. Evidently the colostrum furnishes to the new-born mammal protective antibodies, which probably add much to its capacity to resist infection in early life. If the infant does not receive colostrum it acquires euglobulin in its blood much more slowly, and presumably is in corresponding degree less resistant to infection. It is not probable that there is any equivalent substitute for human colostrum for new-born infants. The findings of numerous recent workers reviewed in this article add force to the statements made by Famulener ten years ago, that it is most highly desirable that every new-born infant should receive its full ration of human colostrum.

(The details of this paper are published in the *Journal of the American Medical Association* **78**:863, Mar. 25, 1922.)

February 13, 1922.

TRANSACTIONS OF THE
CHICAGO PATHOLOGICAL SOCIETY

Vol. XI. June 1, 1922. No. 7

MIXED TUMORS OF UTERUS*

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Mixed tumors of the uterus are derived from embryonal rests of mesoblastic tissue displaced along the course of the wolffian duct. They contain a variety of mesoblastic tissues such as bone, cartilage, smooth muscle, striated muscle, fat and connective tissue. Two mixed tumors of the uterus are described in this report. One of them contains the variety of tissues usually reported, the patient from whom it was removed surgically died within three months after operation with tumor recurrence. The other tumor is almost entirely fatty areolar tissue and at the time of this report (two years after operation) the patient is living and well.

Oct. 10, 1921.

THE KOTTMANN REACTION FOR THYROID ACTIVITY

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Medical problems involved in thyroid dysfunction have come into particular prominence during the last few years. There are several causes of this interest, among which may

* A complete report will be published in the Journal of the American Medical Association.

be mentioned the successful isolation of at least one of the active constituents of the thyroid gland, the development of clinical methods for the study of basal metabolism as well as the more frequent use of therapeutic measures previously seldom employed (irradiation, etc.).

The theoretical premises of the reaction are the following: Kottmann assumed, on the basis of previous work with serum in pregnancy,[1] that certain physicochemical differences must exist in the serum in cases of thyroid dysfunction, and that the chief difference would exist in the state of dispersion of the serum colloids. Because of the peculiar relation of iodin to the glandular metabolism, he began his experiments with colloidal iodin preparations, using silver iodid for this purpose because of its well known photosensitivity. In the test as developed by him, certain phenomena commonly observed in photography play a rôle. Thus, when silver nitrate is added to potassium iodid, silver iodid is formed. In the presence of protective colloid, the growth of the particles is retarded, depending on the protective property of the colloid used. In the photographic plate, a gelatin preparation is used for this purpose, and the prepared film (silver iodid or bromid dispersed in gelatin) is permitted to ripen. During this process of ripening, the colloidal particles of the silver salt gradually become larger and as they do so they become more phosphosensitive than when in the original highly dispersed state. If we substitute serum for the gelatin, a similar reaction might be anticipated, the particles of silver iodid formed becoming larger or smaller according to the protective property of the serum. The greater the photosensitivity of the silver iodid, the poorer the protective property of the serum used, and presumably, therefore, the coarser the collodial dispersion of the serum itself. The less photosensitive the silver iodid, the greater the protective power of the serum and presumably, the greater the state of dispersion of the serum colloids themselves.

TECHNIC

To 1 c.c. of clear serum are added 0.25 c.c. of a 0.5 per cent. solution of potassium iodid and 0.3 c.c. of a 0.5 per cent. solution of silver nitrate. The resulting suspension of silver iodid in the serum is next exposed for five minutes at a distance of 25 cm. to a 500 watt Mazda lamp (or other light of equal intensity). Then 0.5 c.c. of a 0.25 per cent. solution of hydroquinon is added and the color changes observed at five minute intervals.

1. Kottmann, K.: Cor. Bl. f. Schweiz. Aerzte, 1917, Nos. 20, 29, 31.

In carrying out the test, a dark room is theoretically desirable; diffused daylight does not materially interfere with accurate results, according to our experience. The serum used should be freshly drawn, preferably in the morning before food has been taken, and should be free from hemoglobin and quite clear. The test tubes used should be carefully cleaned and of uniform size. We have found that a tube 1.5 by 8 cm. is quite satisfactory in that it permits thorough mixing of the reagents by gently agitating and rotating the tube. The reagents should be freshly prepared and accurately measured. A slight excess of iodid retards the reaction, while an excess of the silver nitrate accelerates the appearance of the color on development.

The color reaction that developes after the addition of hydroquinon varies with different serums. With serum from hyperthyroid cases, Kottmann found that the original yellowish color of the serum mixture persisted for a considerable time; in normal serums a brown color (silver iodid reduced to free silver) makes its appearance quite promptly; in serums from hypothyroid cases Kottmann found the development of the brown color reaction accelerated. The serum from individuals who have had bromids retards the reaction, and such medication must be excluded if the test is to be carried out.

CLINICAL RESULTS

We have studied the test in a relatively large series of cases of thyroid dysfunction as well as in control serums obtained from normal persons and patients ill from a variety of acute and chronic diseases. The material was obtained from the Lakeside Hospital in Cleveland, the Augustana Hospital, the Cook County Hospital, the prenatal clinics of the Michael Reese and St. Luke's hospitals in Chicago, as well as from a number of private patients, and we find that the Kottmann reaction seems to offer an index of thyroid activity, and as such should be of value in clinical work. The test is simple, is rapidly carried out, and if we may judge from the results in the cases here presented, few other clinical conditions yield serums in which the reaction is delayed to a degree at all comparable with the reaction obtained with exophthalmic serums. Some retardation is noted in other conditions, such as cachexia, and occasionally in pregnancy and in severe excitement, but these conditions should in no way interfere with the clinical interpretation of the test. In only a few cases of clinically active hyperthyroidism was the typical reaction absent (three out of seventy).

Oct. 10, 1921.

THE PATHOLOGY OF LOOSE BODIES IN JOINTS

D. B. PHEMISTER

There are several varieties of loose bodies in joints, the two most important of which are those arising from the synovial lining and those arising from the articular surfaces of the bones. The pathogenesis of both forms is still poorly understood. Those of synovial origin arise by a process of chondrification and ossification in the villus tags of the joint. Kölliker demonstrated cartilage cells in many of the normal villi of the joint, and Rainey advanced the theory that under certain influences, either as a result of inflammation or as a tumorous process, such villi proliferate, forming cartilaginous nodules which at first are attached by a pedicle, but later may become detached, giving rise to loose bodies in the joints. The condition is usually spoken of as chondromatosis of the joint, and the masses are usually multiple, sometimes numbering several hundred. They usually undergo more or less extensive calcification and ossification, and growth may continue after they are completely detached.

Loose bodies arising from the articular surfaces of the ends of the bones constitute by far the most frequent and important group. They nearly always occur singly and when multiple rarely number more than two or three. They occur in the knee joint in the great majority of cases, the elbow being the only other joint that is at all frequently involved. The condition is limited largely to young adult males. The loose body at the time of its detachment may consist of a portion of articular cartilage alone or of articular cartilage with underlying bone. The most frequent point of origin in the knee joint is the lateral margin of the mesial condyle of the femur. It is occasionally the inferior articular surface of the patella or the anterior articular surface of the tibia. There has been much dispute as to the method of origin. Barth claimed that in a majority of cases bone or bone and cartilage is chipped

off by trauma. König claimed that there is usually a primary disease at the point of origin, the exact nature of which is unknown but which leads to the formation of an absorption zone with separation and sloughing off of the affected region into the joint. Trauma may be the exciting factor in some instances. Axhausen has taken a middle position between Barth and König, claiming that there is first traumatism to the involved region, which interferes with its blood supply and results in aseptic necrosis of the cartilage alone or cartilage and underlying bone. Instead of organization and substitution of necrotic portions, as results from aseptic tissue necrosis in other regions, there is formed a zone of absorption with subsequent detachment and extrusion into the joint of the damaged portion. A second and usually slight trauma may dislodge the partially detached piece from its bed.

The following case speaks strongly against this theory and in favor of the view of König that the process is one of osteochondritis dissecans of unknown etiology.

Male, aged 21 years. No previous trouble with knee. While lying with limb in extension he experienced a sharp pain in left knee and immediately felt loose body in lateral portion of joint. Roentgen ray showed shadow of body in suprapatellar region and a corresponding defect in inferior articular surface of patella. Removal three days later. Bloody fluid in joint. Loose body consisted of articular cartilage and underlying bone. Central portion of cartilage showed a fresh fracture surface where it had become detached from patella, but peripheral portion and the surface of the attached bone showed evidence of old separation with a thin fibrous covering. Microscopic examination showed living bone cells filling all of the bone lacunae and a layer of fibrocartilage covering practically the entire extent of the bony surface along the line of separation. There were some areas of necrosis in the articular cartilage. The great majority of its cells showed no evidence of necrosis. In this case it is impossible to conclude that detachment followed as a result of necrosis of the loose body, because all of its bone and nearly all of its cartilage were alive.

After detachment all bony portions undergo necrosis if they have not previously done so, but superficial por-

tions of cartilage survive and proliferate. A layer of fibrous cartilage forms over the bony surface and eventually the bone becomes completely surrounded by cartilage. Calcification usually takes place in the deeper portions of the cartilage and absorption with replacement of the dead bone is slowly accomplished by the surrounding cartilage. In the course of years there may be extensive cartilaginous growth with considerable increase in size of the loose body. A peculiar type of ossification may occur in the calcified zones. These bodies are an excellent example of tissue culture in vivo.

Jan. 9, 1922.

CULTURAL DIFFERENCES AMONG ACID-FAST ORGANISMS

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For a short time after Koch's discovery of *B. tuberculosis* and Ehrlich's discovery of that phenomenon which we call its acid-fastness it was supposed that tubercle bacilli and Hansen's leprosy bacillus were unique in this staining property. But in 1884 Lustgarten, finding acid-fast bacilli in the neighborhood of specific urogenital lesions, announced that he had discovered the cause of syphilis. His startling claim was quickly disproved, but he remains on record as the discoverer of the smegma bacillus, now long since known as a widely distributed acid-fast saprophyte. From time to time after this, acid-fast bacilli were seen, if not isolated, and their pathogenicity and relationship to the tubercle bacillus speculated upon.

The year 1897 was a fruitful one in the discovery of these organisms. It was then that Moeller isolated the dung bacillus from cattle feces, and that Petri and Rabinowitsch discovered nonpathogenic acid-fast bacilli in butter. And a more exciting report was that of Bataillon, Dubard and Terre concerning the isolation of an acid-fast bacillus from a nodule the size of a pigeon's egg in the abdomen of a carp, an organism

which differed from tubercle bacilli hitherto described in its much more rapid growth and its lower optimum temperature. In the following year with Moeller's highly interesting finding that acid-fast bacilli were not at all uncommon quite dissociated from an animal environment, maintaining an entirely saprophytic existence upon various types of grass, the main types of acid-fast bacilli as we know them today were known.

Aside from tubercle bacilli and the leprosy bacillus of Hansen, about forty supposedly different acid-fast bacilli have been described. In general these differ from tubercle bacilli in two respects, their relatively rapid growth and the lower temperature at which they thrive. Although many of them are unquestionably identical, certain vaguely defined groupings based on cultural differences as well as difference in habitat have been established. It is these that I shall discuss.

Distinctions among acid-fast organisms are of immediate and also of far reaching importance. When it comes to a question of kidney extirpation it is a matter of no small concern to the patient to know if the acid-fast bacilli detected in his urine are smegma bacilli or true tubercle bacilli, and no milk dealer, however scrupulous, could view without protest the discard of many dollars worth of his product because it contained a few detectable butter or grass bacilli.

But the subject merits consideration from a far broader point of view. Rightly or wrongly on the basis of this single attribute of acid-fastness the organisms so endowed have been classified as a distinct biological group, and more than one investigator has tried to trace a close phylogenetic relationship between them. A frequent assumption concerning their relationship is derivation of all of them from a common acid-fast ancestor. And a battle royal is still being waged as to their transmutatability, or at least the conversion of avirulent types into pathogenic forms by repeated animal passage. There are those who stoutly maintain the latter possibility, opposed in turn by a larger group who believe in a far more sure fixation of type, and a difference in virulence at least as marked as that between typhoid bacilli and colon bacilli.

The practical importance of the question, as we see, centers around the problem of virulence. Now virulence, in turn, depends on two chemical factors, first, the ability of the invading organism to resist the defenses of the host, which are chiefly lytic in nature, and secondly, its ability to obtain a food supply in that environment. To a certain extent the first of these factors is a matter of chemical composition, while the second is a function of metabolism.

Now chemical composition certainly plays a rôle in the resistance displayed by all these bacilli to intracorporeal digestion. As is well known, all of them excite on injection into living tissues a typical foreign body response. With most members of the group the process remains local; the tubercle bacillus, on the other hand, is a multiplying foreign body and elicits the same response on its spread. The multiplication of a foreign body in tissues is the criterion for virulence. The mere persistence of intact bacilli and excitation of a localized foreign body reaction, do not constitute disease, and may in fact occur following the introduction of dead tubercle bacilli as well as living avirulent organisms, a fact which has been overlooked by not a few transmutationists. The typically inert foreign body rôle played by members of this group when in tissue is not hard to explain. As compared with the nonacid-fast bacteria, all of them are characterized by a signally high lipoid content, approximately 35 per cent. of the dry weight. The lipoid is frequently waxy in nature and therefore highly resistant to digestion. And we are beginning to get evidence that the lipoid of the tubercle bacillus is the most waxy of all of them. Mr. Campbell and I have found that while tubercle, smegma and grass bacilli all contain about the same amount of lipin and have about the same saponification number, the proportion of the total lipin present as nonsaponifiable solid alcohol is distinctly lower in the saprophytes than in the true tubercle bacillus, from 5 to 10 per cent., whereas as high as 40 per cent has been reported for the tubercle bacillus (Kresling). It is too early to say if when we get all our acid-fast strains analyzed we may be able to correlate this factor up with virulence.

It is the other factor, that of nutrition and metabolism, that I wish more particularly to consider. Certain gross differences in the manner of growth should perhaps be recalled first. Tubercle bacilli of the human and bovine types are slow growers on glycerol broth or agar, about a month being required to secure a satisfactory culture. The product of growth is raised, dry and granular, and in old cultures slightly yellowish. The avian type bacillus grows rapidly on the same media in a slimy smear and is nonpigmented. The leprosy bacillus—isolated from leprous lesions, but still of doubtful etiological significance—is a pigmented organism growing rapidly as a slimy film. Frog, fish and turtle bacilli grow in a manner similar to the avian bacillus, but even more profusely, and differ from the other acid-fast bacilli in that they thrive best at 25 degrees, while the others do best at body temperature. Smegma bacilli reproduce rapidly as a greasy film, not colored and becoming more tenacious with the passage of time. Unlike the avian bacilli, the leprosy bacilli and the bacilli of cold blooded animals, the smegma bacillus may readily be floated on broth and made to grow as a rapidly spreading, rather dense film. The grass bacilli of various types grow rapidly at incubator temperature, and almost as rapidly at room temperature, in a dry and granular form, and can readily proliferate as a thick film on glycerol broth. They are the easiest acid-fast bacilli to obtain in quantity.

Up to the present the chief distinctions within the group have been based on virulence and isolation history. It has seemed to me for some time that virulence and habitat in nature should both be correlated with their manner of obtaining food. On this basis we ought to be able, perhaps, to bring out identities among avirulent organisms of different isolation history, and on the other hand distinguish between organisms otherwise similar. My method of attack has been simply trial of growth of the various members of the group with simple chemical compounds as sole source of carbon and nitrogen. In their capacity as chemical reagents bacteria should be distinguished by their action on various chemicals, and the particular action I have looked

for so far is the very complicated but easily recognized one of ability to build up their entire protoplasm from the simple chemicals provided, in other words, grow and multiply.

Now as you will see, many discrepancies have crept into the results, which I explain on the ground that bacteria, while chemical reagents, are not pure reagents, and so lead to errors which can be eliminated only by the *sine qua non* of biological research, control and repetition. I still believe that in spite of the inconstancies which you will note in my tables many of you will agree that they are as reliable as those still more complex chemical reagents, guinea-pigs.

Table 1 shows the availability of nitrogen in various forms for certain acid-fast organisms. The carbon requirement is satisfied by glycerol, and inorganic salts, including the indispensable phosphates, are supplied in appropriate amount. As you see, the amino nitrogen of alanine suffices as the sole nitrogenous nutriment for all organisms except avian bacilli. The unavailability for avian bacilli is precisely one of the discrepancies I am unable to understand, as the amino group of other amino-acids, as leucine, is utilizable. You will note too that the acid amide nitrogen of propionamide is also generally available, there being only one exception. I should add that all of these experiments were run in quadruplicate, and that in case of such exceptions the whole experiment was repeated. The peculiarity in the cases under consideration remained constant. Whether it would do so after another year of culture I am not prepared to say.

Ethyl amine you will noice was a suitable source of nitrogen for but a very few, certain grass bacilli and the frog bacillus. The surprising fact is that it is available for any, as primary amines are stable substances in the presence of most chemical reagents.

Ammonia is of course suitable for all. It is probably largely by conversion into ammonia that the nitrogen of any compound becomes available for bacterial synthesis.

Creatinine, which has imino (—NH—) but not amino ($—NH_2$) nitrogen furnishes available

nitrogen for grass, mist and smegma bacilli, for the bacilli of cold blooded animals and for one of the leprosy bacilli, but is unsuitable as a source of nitrogen for tubercle bacilli. Here is a distinct difference, which brings out what we may consider a rather general characteristic of saprophytic life, ability to produce a more vigorous cleavage of complex substances than that possessed by pathogens. It is by saprophytes of course that the great carbon and nitrogen cycles are maintained. The pathogens are apt to be sticklers for predigested food.

There is something rather striking in the availability of urea nitrogen, this compound being a suitable source of nitrogenous nutriment for about the same group. It will be noted that in both cases the lepra bacilli and the bacilli of cold blooded animals behave like the unquestioned saprophytes, with one or two exceptions. I should say at this point that I consider the mist or dung bacillus a grass bacillus which has become a dung bacillus purely as a result of an involuntary trip through a cow's alimentary canal, and not as a result of any choice of habitat.

Table 2 depicts a study in carbon metabolism. It shows the availability of the carbonaceous residue which might be left from amino-acids after the abstraction of nitrogen. You will recall that in the presence of glycerol, which is a suitable source of carbon for tubercle bacilli, these bacilli were able to thrive with the nitrogen of alanine. But now, with the glycerol left out, no growth occurs. The condition is the same all the way down the line. Carbon in a variety of forms, perfectly siutable for the growth of the other organisms in most cases, is not in the right form for tubercle bacilli. The glycerophilism of the tubercle bacillus is its most distinctive cultural trait.

It will be noted in addition that the aromatic ring compounds, tryptophane, phenyl-alanine and tyrosine, are practically unavailable as sole sources of carbon and nitrogen. Their nitrogen is perhaps in an available form, but the products left after its abstraction, which are of the general group loosely called phenol bodies, are probably too toxic to permit growth, or are

TABLE 1.—GROWTH ON AMINO, AMIDE, AMINE, IMINO, AND AMMONIA N (THE MEDIUM CONTAINS GLYCEROL)

Nitrogen	H37	H102	R1	B1	A1	A2	Lepra Hardy	Lepra Duval	Frog	Turtle	Fish	Smegma N.W.	Smegma S.L.	Smegma Grass	Grass III	Grass IV	Mist	Timothy
Alanine	++	+	·	++	0	0	++	+++	+++	++	++	+++	+++	++	+++	+++	++	++
Propionamide	+	++	+	+	+++	+	+	+	+	0	+	++	++	++	+	+	++	+
Ethylamine (HCl)	0	0	0	0	0	..	..	0	+	0	0	..	0	0	++	++	0	0
Ammonia (HCl)	+	++	+	++	++	++	..	+	+	+	+	..	+	+	..	..	+	+
Creatinine	0	..	..	0	0	0	+	0	+	+	+	+	++	++	+++	+++	++	++
Urea	0	..	..	0	0	..	++	++	+	0	0	++	++	++	++	++	++	++

TABLE 2.—GROWTH ON AMINO ACIDS WITHOUT GLYCEROL

Amino-Acid	H37	H102	R1	B1	A1	A2	Lepra Hardy	Lepra Duval	Frog	Turtle	Fish	Smegma N.W.	Smegma S.L.	Smegma Grass	Grass III	Grass IV	Mist	Timothy
d-l Alanine	0	0	0	0	0	0	+	+	++	++	++	++	++	++	++	++	++	++
Leucine	0	..	..	0	0	..	..	+	++	++	++	..	+	..	+	..	..	+
Histidine	0	..	..	..	0	0	0	0	0	0	0	++	++	+	++	++	+	0
Tryptophane	..	..	..	..	0	..	..	0	0	0	0	..	0	0	0	..	..	0
Phenylalanine	..	..	..	..	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Tryosine	0	0	0	0	0	..	..	0	+	..	..	..	0	..	..	..	..	0

TABLE 3.—GROWTH ON AMMONIA + VARIOUS SUBSTANCES CONTAINING CARBON

Nutriment	H37	H102	R1	B1	A1	A2	Lepra Hardy	Lepra Duval	Frog	Turtle	Fish	Smegma N.W.	Smegma S.L.	Smegma Grass	Grass III	Grass IV	Mist	Timothy
$NH_4Cl + C_2H_5OH$	0	..	..	..	0	0	..	0	+	0	0	..	+	+	+	+	+	+
$NH_4Cl + CH_3OH$	0	..	..	..	0	0	..	0	0	0	0	..	0	0	0	0	0	0
NH_4Cl + glycerol	++	++	+	++	++	++	..	+	+	+	+	..	+	+	..	..	+	+
NH_4Cl glycol	0	..	..	0	0	..	..	0	0	0	0	..	0	0	..	..	0	0
NH_4 propionate	0	0	0	..	0	0	0	0	++	++	0	++	++	++	++	++	++	++
NH_4 acetate	..	..	..	..	0	0	..	0	0	0	0	..	0	0	..	..	0	0
NH_4 lactate	0	0	0	0	0	0	0	..	++	0	0	++	++	++	++	++	++	+
NH_4 glycolate	..	..	..	..	0	0	0	0	0	0	0	0	0	0	0	0	0	0
NH_4 pyruvate	0	0	0	0	+	0	++	+	++	+	++	+	++	+	++	++	++	++

not readily broken up themselves to yield straight chain carbon for nutrition. This does not mean that in the presence of other carbon nutriment these amino-acids may not be very useful in small quantity *per se*. Their presence would save a certain amount of synthesis in the construction of bacterial protein, but it should be added that each of these organisms is quite able to synthesize its own ring compounds from very simple straight chain material.

The situation with histidine is worth comment. Histidine suffices as sole source of nitrogen and carbon for the smegma bacilli and grass bacilli with one exception. In this case, in contrast to what we have seen before, the leprosy bacilli and bacilli of cold blooded animals behave more like tubercle bacilli than like the unquestioned saprophytes.

Table 3 shows another study in carbon metabolism. You will recall that ammonia was a suitable source of nitrogen for all of the group. Glycerol is likewise for all a sufficient source of carbon. It is, of the substances studied, the only suitable sole source of carbon for tubercle bacilli. The chief point, in addition to this, brought out by this table, is the availability of the three carbon atoms and nonavailability of the two carbon ones, and the corresponding situation with those alcohols which for a number of chemical reasons may be considered corresponding alcohols, ethanol and methanol. This is quite sharp and must represent a situation fundamental in nutrition; but we have time tonight only to call attention to it.

From the considerations pointed out it seems to me that a tentative grouping within the acid-fast group may be made on the basis of nutrition. In the first place the true tubercle bacilli ,including human, bovine and avian types, are at once set apart by the fact that glycerol is so important in their carbon nutrition. Another group which is fairly well defined includes the smegma bacilli and grass bacilli of various types, which in a way behave similarly toward most of the compounds studied, and are on the whole more readily adapted to a restricted diet than tubercle bacilli, and also better able to cope with a diet made up entirely of

a single complex compound like creatinine. This separation leaves the lepra bacilli—provisionally so called—and the tubercle bacilli of cold blooded animals—also provisionally so called. As you may know, Weber and Taute and Krause hold it not unlikely that the last group is really nothing more than grass bacilli introduced one way or another into sites of lowered resistance in cold blooded animals, there to multiply slowly and after a while take on some new cultural characteristics. As far as my results go—such as their utilization of the carbonaceous portion of alanine and leucine as the sole source of carbon, on the one hand, and their less ready utilization of propionic and lactic acids and of ethyl alcohol on the other—they exhibit rather distinct cultural differences from both tubercle bacilli and the saprophytic smegma and grass bacilli. Furthermore in not a few cases they have cultural characteristics in common. Cautiously we might for the present let them rest together in a third group of their own.

Jan. 9, 1922.

RHABDOMYOMA OF THE LUNGS OF A SHEEP

L. ENOS DAY

Tumors which are composed principally of striated muscle fibers are of rare occurrence, and especially so in organs other than those of the genito-urinary system.

With reference to form, Ewing states that they may appear as single or multiple, nodular or voluminous, flat or rounded, circumscribed or diffuse, and even polypoid growths. This statement is supported by most of the writers. They are usually soft and of a gray color on section, mottled with tiny bands of a slightly darker color, which lie in an abundant connective tissue stroma, although cystic forms have been reported.

Rhabdomyomas usually occur in early life, most of which are probably congenital, yet there have been exceptions. Fujinami observed one in a patient 50 years of age, and Wolf in a patient 75 years of age.

These neoplasms are generally considered as non-malignant, yet there have been instances in which metastases were observed. Malignancy in these growths appears to depend wholly on the presence of rapidly growing muscle cells.

The subject of this report, a lamb, 4 or 5 months old, was slaughtered at one of the large packing establishments in Chicago, some time ago. The sex and breed were not recorded at the time of slaughter. Upon evisceration, both of the lungs were found to contain perhaps a thousand or more spherical nodules, which ranged in size from 1 mm. to 2.5 cm. in diamter. A cut surface through the greatest diameter of the caudal lobe of the right lung exposed 185 of these growths, which were quite evenly distributed through both lungs. Some of the large growths were situated just beneath the pleura, but did not appear to involve this membrane. Generally speaking, the peripheries of the neoplasms were comparatively smooth, yet some of the larger ones showed a few bosselations on their surfaces, which appeared to be an outgrowth of tumor substance. In a few places there was a coalescence of two or more tumors. On incising they were fairly firm, but not firm enough to suggest a preponderance of fibrous tissue. The cut surface was pinkish gray, slightly mottled with short bands of a slightly deeper pink.

The lungs appeared normal in size, and the lung tissue which was not involved in the new growths seemed normal in color and texture. All other organs were reported normal by the inspector who conducted the autopsy.

Specimens for microscopical examination were taken from some of the larger as well as some of the smaller growths, as it was desired to secure sections which would be representative of all. The specimens were fixed in Zenker's fixing fluid and later embedded in paraffin. Sections were cut about 5 microns in thickness, stained with Harris' hematoxylin and eosin. A few sections were stained with phosphotungstic acid hematoxylin with very good results.

In viewing the sections under low magnification, a large number of long cells, grouped in bundles, extended in all directions. In places the bundles were of even thickness throughout and were woven together in basket fashion; in other places the bundles were fan shaped and were lodged in what appeared to be a stroma of small, round and more or less irregular cells, which constituted not more than 25 per cent. of the field. Scattered through each field were from six to eight circular openings lined with large cuboidal cells. At first these were thought to be atrophic bronchioles. In

sections from some of the larger growths bronchioles were encountered. In these instances the bronchiole appeared normal, with the exception of a collection of small cells between the epithelial and muscular coat and an edema of the wall and around the periphery of the bronchioles.

When higher magnification was used (about 350 diameters) the long fusiform cells which made up the bundles were found to be young, undeveloped, striated muscle cells, which were arranged quite orderly. Some of the muscle fibers were not striated; in others only a part was striated; that is, one end of the fiber was striated, while the other end was smooth. Others showed pale striations in the middle and the ends were smooth, and still others had pale striations along one side of their axis and the other side smooth. In many places there were both long and short fibers in the same field; also narrow and broad. The longest measured about 320 microns. The striations were about 2 microns apart. The broadest fiber encountered was 8 microns, while the narrowest was 2 microns. No definitely branched fibers were encountered. Some pear-shaped as well as spherical-shaped cells were seen. All of the muscle cells were devoid of sarcolemma. The nuclei were located in or near the center of the cell and never on the surface as in the adult striated muscle fibers. The cell protoplasm was homogeneous. No glycogen droplets were seen as mentioned in cases of rhabdomyoma reported by Wolfensberger, Broch and Hibbert. These authors report observing glycogen droplets around the nuclei.

The muscle fibers seemed to be quite evenly distributed throughout the growths. There were very few cells other than muscle cells and cells lining tubules, which will be referred to later, encountered in the sections. Owing to the large number of small round cells present in rhabdomyomas in other locations of the body, some writers have suggested the term rhabdomyoma sarcomatoides. Since only a very few such cells were present in these growths, one could not look upon them as belonging to this class of new growths, but as a rhabdomyoma in the strictest sense of the word. Scattered through the growth were a large number of gland tubules, the lumen of which was from 10 to 180 microns. These tubules were lined with a single row of cells which appear to be epithelial in character and resemble somewhat those lining the tubules of the kidneys, only not quite so well differentiated.

The epithelium of the bronchi and bronchioles was well differentiated. There is an increase of lymphocytes between the mucous membrane and the nonstriated muscle. The muscular coat of the epithelial lining does not appear to take any part in the growths whatever.

Rhabdomyoma in the lower animals is quite rare. The only cases mentioned that I have been able to find are by Kitt in his textbook of comparative and general pathology. He stated that John has recorded an adenosarco-rhabdomyoma in the kidney of a hog which weighed fourteen kilograms or about thirty-one pounds. From the large size of this growth coupled with my observations of new growths in the kidney of swine, I would be inclined to look upon this growth as an embryonal adenosarcoma, as these growths are of a very mixed character and striated muscle fibers have been observed in them. Of the remaining two, Gratia observed a rhabdomyoma in an old horse in a dissecting room; a fusiform growth about 8 to 10 centimeters in length in the vagus nerve trunk about the middle of the neck. The other was found by Kolessnikow growing in the tail and perianal connective tissue of a 20-year-old stallion. This tumor contained pigment cells to which the name rhabdomyosarcoma melanodes was given. Metastases were found in the liver, skin, pleura and peritoneum.

Concerning the histogenesis of the growths in this particular case and the explanation of the presence of the gland tubules, I am of the opinion that they sprang from misplaced embryonal tissue. The gland elements are probably remnants of the Wolffian body, while the striated muscle cells probably spring from inclusions of the myotome, which were not separated at the proper place in early embryonal life.

Feb. 13, 1922.

THE RELATIVE TOXICITY OF FETAL AND MATERNAL PLASMA*

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SUMMARY

Blood plasma obtained from pregnant women is more toxic for the guinea-pig on intravenous injection

* Original articles appear in the Journal of Immunology.

than plasma obtained from normal individuals. Human placental plasma is practically nontoxic. Similar relations are found with dog plasma obtained from pregnant dogs and from full term fetuses.

Plasma obtained during the menstrual cycle (before and after) is occasionally more toxic for the guinea-pig than normal female plasma.

The cause of death in the guinea-pig is an intravascular clotting in the capillaries of the lungs, with a resulting asphyxia, and occlusion in other capillaries as well (brain, etc.). Death can be prevented if the animal is hirudinized, or if the amount of citrate simultaneously injected, is increased.

Feb. 13, 1922.

SEROLGIC AND BIOLOGIC RELATIONS OF B. COLI FROM RENAL INFECTIONS TO STRAINS ISOLATED FROM FECES AND THE CERVIX UTERI

RUSSELL D. HERROLD

It was thought that the correlation of strains of B. coli from various sources in the same patient with the strains concerned in a urinary infection might aid in determining the probable source of the urinary infection, since colon bacilli have been generally found to be a heterogeneous group. This comparison was made by means of serologic and biologic methods.

Eight women with acute pyelonephritis were observed. Blood agar plates were inoculated with smears from throat, feces and cervix of uterus. Stock cultures were selected from each plate and a preliminary classification made into hemolytic or nonhemolytic according to the change produced on blood agar plates.

Monovalent serums were then prepared with each urinary strain by injection of rabbits intravenously, and cross agglutination tests were made with the cultures from various sources.

Further observations were made on the relation between hemolytic property and fermentation. A com-

parative clinical summary of a series of hemolytic and nonhemolytic renal infections was also made.

The following conclusions were reached: Colon bacilli can be isolated frequently from the cervix of the uterus and from feces of patients with renal infections which correspond in serologic and biologic tests to the bacilli from the urine of the infected kidney. Some hemolytic colon bacilli were found to belong serologically in one group. The hemolytic property is not accidental but persists during weeks of infection in the urinary tract as well as on artificial mediums. There is no definite relation between hemolysis by colon bacilli and their fermentation of sugars. The incidence of hemolytic colon bacilli in renal infections is greater than generally known, and this type of bacillus has a somewhat greater average of virulence than the nonhemolytic but the latter appears to persist longer.

Feb. 13, 1922.

BACTERIOLOGY OF SYSTEMIC INFECTIONS CAUSING DEATH FOLLOWING MISCARRIAGE OR ABORTION

WILLSON B. MOODY

From The John McCormick Institute for Infectious Diseases and Laboratory of the Cook County Hospital

This report is based on the bacteriological examinations of body fluids and organs removed at autopsy of twenty-eight patients dying in the Cook County Hospital of systemic infection following miscarriage or abortion. It covers a period between May, 1920, and January, 1922, and is part of a study of the pathogenesis and pathological anatomy of sepsis resulting from miscarriage or abortion, spontaneous or criminally induced. Rather extensive study has been made of the bacteriology of puerperal sepsis but it is only during the past ten or twelve years that much attention has been paid to the bacteria found in patients with evidence of systemic infection following miscarriage or

abortion, and nearly all such investigations have been studies of the relation of the bacteria found to the prognosis and treatment, rather than to the pathological anatomy.

Schottmüller [1] in 1910 made a study of the cervical flora of 100 cases of septic abortion and isolated in largest numbers such organisms as S. erysipelatis, staphylococcus, B. coli and pneumococcus. Winter [2] the following year reported similar results and determined the course of treatment by the bacteria isolated. Numerous papers continued this discussion concerning the bacteriology and treatment and it seems that the majority of investigators were unable to correlate the clinical course with the bacteria found in the cervical secretions. It does appear, however, that the hemolytic streptococcus is not commonly present in the cervical or uterine secretions and also that when systemic infection following abortion or miscarriage due to this organism occurs, the course is shorter and the mortality higher. Traugott [3] included in his study of the bacteria of the lochia in septic abortion, the results in six deaths. S. longus was isolated three times. B. coli and a diplostreptococcus twice, and staphylococcus albus and a diplostreptococcus once. Thrombophlebitis, infarction and endometritis or parametritis were found in those instances where S. longus was the predominating organism; with infections due to colon bacilli and staphylococcus there was more suppuration; pelvic peritonitis, purulent parametritis, and peritonitis being noted. Warnekros [4] in seven deaths from sepsis following abortion found streptococci in the peritoneal fluid or heart blood in nearly every instance, though with three there was a mixed infection. Thrombophlebitis was present in three, and S. longus isolated each time. In ten cases there was one with peritonitis,

1. Schottmüller: Zur pathogenese des septischen abortes, Münch. med. Woch., 1910, Vol. lvii, 1817-1819.
2. Winter: Zur Prognose und Behandlung des septischen Abortes, Zent. f. Gynak., 1911 xxxv, 569-76.
3. Traugott: Zur Frage der Bakteriologie and der lokalen Behandlung des fiebernden Abortes, Zeitsch. f. Geburt. u. Gynäk., 1911, lxviii, 328-52.
4. Warnekros: Zur Frage der Behandlung des fieberhaften Abortes, Arch. f. Gynak., 1912, xcviii, 600-15.

four with peritonitis and sepsis, five with sepsis and pyemia. Hemolytic streptococcus was found in the peritoneal fluid four times, and staphylococcus once. Warnekros found that organisms isolated from the blood were often different from those in the lochia.

The present study deals with material collected by Dr. E. R. Le Count at the postmortem examination of bodies of the patients dead from sepsis following miscarriage or abortion, twenty-eight cases in all. In nearly all, cultures were made of the blood from the heart, of peritoneal, pleural, pericardial and cerebrospinal fluids, splenic pulp and uterine contents; in all, stained direct smears were made. Blood agar plates for aerobic and anaerobic bacteria were prepared, and dextrose boullion was also inoculated.

Hemolytic streptococcus was isolated as the predominating organism in thirteen instances, B. coli in four, staphylococcus in four, pneumococcus in three, B. proteus in two, B musosus capsulatus in one, and alpha streptococcus in one. Mixed infections were encountered in various fluids, but the bacteria as mentioned were found in each case in several of the materials examined.

Blood from the heart was cultured twenty-seven times with positive results in twenty-two instances. The streptococcus was found seventeen times, B. coli and staphylococcus four each, pneumococcus three, proteus, pyocyaneous and alpha streptococcus each once.

Cultures of fluid obtained from the peritoneal cavity remained sterile in five out of twenty-one instances. B. streptococcus was isolated in eight instances, pneumococcus, B. coli, staphylococcus each twice, alpha streptococcus and B. mucosus capsulatus each once.

It is of interest to note that twice large numbers of gram positive cocci were seen in cover glass preparations of peritoneal fluid but repeated cultures in solid and fluid media failed to yield any such organisms.

Six of twenty-three cultures of spinal fluid remained sterile, beta streptococcus was isolated in five instances, staphylococcus in six; pneumococcus and B. coli two; pyocyaneous and B. mucosus capsulatus each in one.

Fluid from the pleural cavities was cultured in twenty instances yielding beta streptococcus ten times; B. coli and staphylococcus each three; pneumococcus twice, proteus and streptococcus one.

From twenty cultures of the spleen, nine remained sterile. Five contained beta streptococcus; two B. coli; one each pneumococcus, staphylococcus, proteus and streptococcus.

Material from the cavity of the uterus was used for cultures in fourteen instances; from two uteri nothing grew, six contained beta streptococcus, two each B. coli and staphylococcus, and one each proteus and streptococcus.

Although from many bodies more than one organism was recovered from the material, from the majority some one type of bacteria was found in several of the fluids examined. Summarizing the results of the twenty-eight cases, there were twenty-four in which some one organism appeared in several of the fluids from the body, thus beta streptococcus was isolated from more than one place in thirteen, pneumococcus, B. coli and staphylococcus in three each, B. mocosus capsulatus and streptococcus each in one. Cultures during life were made from the blood of five patients. In only one were any organisms found: these were beta streptococci and in this case there was thromboulcerative endocarditis.

The hemolytic streptococci isolated in all instances proved to be of the beta type; all fermented lactose and salicin but not mannite nor inulin and efforts to determine any specific strain by agglutination tests failed. Agglutination of suspensions of these strains by serum from rabbits injected with strains of hemolytic streptococcus from several sources such as scarlet fever, erysipelas and infected tonsils as well as postabortion sepsis failed to show any specific characteristic group.

It was noted at the postmortem examinations, that the alterations were, as a rule, a peritonitis or a thrombophlebitis of varying locations, degrees and sequences but these two sorts of alterations were rarely combined.

A difference in the bacteriology to correspond to the two types of alterations was not definitely established.

Statements, particularly in the negative, by patients who have criminal or self-induced abortion are entirely unreliable. Admissions were obtained from thirteen patients, that pregnancy was interrupted by a midwife, a physician, or the patient herself. In four of these patients hemolytic streptococcus were found; in seven staphylococcus or B. coli; and pneumococcus and proteus each once. In three of the four cases where beta streptococcus was found it was stated that a physician or midwife had introduced rubber balloons or performed curettage. In the fourth, the patient stated that she had inserted a slippery elm stick, but it was later found that the uterus was perforated. Patients with sepsis associated with such organisms as B. coli or staphylococci or B. proteus were apparently treated under conditions far from aseptic and with repeated introductions of instruments into the uterus.

One patient aborted four days before entrance to the hospital and lived only two days after admission. At the necropsy gangrenous endometritis and acute serofibrinous peritonitis were found, bilateral pleuritis and pyosalpinx. From the blood from the heart, and the peritoneal, pericardial, pleural and cerebrospinal fluids there was a pure culture of hemolytic streptococci.

Two patients denied any instrumentation of the uterus but stated that they had taken pills and used repeated douches to terminate pregnancy. Both were ill about three weeks with cramps, chills and fever. At the necropsy, gangrenous endometritis, fibrinopurulent peritonitis and perimetritis were found. In one instance there was in addition suppurative thrombophlebitis of the right iliac vein, with infarcts in the spleen and in one lung. Cultures of the blood, pleural and peritonal fluids contained beta streptococci.

Another patient had been attended by a midwife and doctor on a number of occasions, later developing chills, fever, sweats and swelling of the left leg, with beginning gangrene. After death a purulent endometritis with an abscess in the myometrium was found, with thrombosis of the uterine, ovarian, renal, iliac, and

femoral veins and inferior vena cava. Staphylococci and B. coli were isolated from the blood in the heart and the inferior vena cava. No organisms were isolated from the peritoneal fluid.

SUMMARY

From this study of the bacteria found in the bodies of individuals dying from sepsis following abortion, it appears that the hemolytic streptococcus is more often found than other organisms, but that such bacteria as B. coli and staphylococci are not infrequently present. It is possible that the hemolytic streptococci are present in the lochia but it appears that some outside influence such as trauma from instrumentation, douches, and the like are necessary to bring about generalized infection.

March 13, 1922.

LIVER CHANGES IN MUSHROOM POISONING*

PAUL KLEMPERER

From the Department of Pathology Loyola University School of Medicine

In the last few years I have had the opportunity of observing a large number of cases of poisoning due to amanita phalloides.

The histological findings in the acute cases (exitus one and one-half to five days after eating of mushrooms) consist of general fatty changes in all the liver cells. In the early fatal case, death occurring before a day, small drops of fat were found, in cases of longer duration large drops flowing together and filling the cells; the fatty substance was not double refractive. In the very first days cell necrosis was present, in the older cases necrosis was more prominent. This does not involve at any time a very large area of the lobules, but remains restricted to distinct small groups of the liver cells, both in the periphery and in the center of the lobules. Besides these regressive degenerative

* Appeared in extenso Virchows Archiv, Vol. 237, p. 401, 1922.

changes, we found in an early phase changes indicating a reparation, as liver cell regeneration and bile duct sprouts in the periphery of the lobules. In contrast we found in cases with a protracted course (death eight to twenty-three days after poisoning) extensive cell necrosis in the center and in the intermediate zone, whereas a broad zone of cell reparation appeared in the periphery of the lobules.

The changes in the liver in acute mushroom poisoning resemble those of phosphorus poisoning, but the subacute mushroom liver suggests, on the first glance, a close resemblance to the liver in acute yellow atrophy. A careful histological analysis, however, proved profound differences between these two processes. These differences may be summarized in the following statement: A coexistence of fresh cell necrosis in the central areas of the lobules and a widely extensive cell regeneration in the periphery as in the subacute cases of mushroom poisoning is not comparable to any stage of the genuine acute atrophy. The fact that the necrosis is of very small extent in acute mushroom poisoning leads to the conclusion that the extensive cell necrosis in subacute mushroom poisoning cannot be considered as a direct result of the mushroom poisoning but only as a result of disturbance of the metabolism of the liver cells appearing in a protracted course of poisoning. The nature of this disturbance of metabolism is quite obscure. Considering, however, the great resemblance of the histological liver changes in acute mushroom poisoning to those of the phosphorus poisoning, we may be entitled to connect some results of the experimental pathology of the phosphorus poisoning with mushroom intoxication. Nenubanuer and especially Frank and Isaac have established that there is a disturbance of the glycogen fixation in the first stage of phosphorus poisoning: the liver cells consume the glycogen very fast in their own metabolism. In the second stage there is an alteration of glycogen formation inasmuch as the liver cell is deprived of its entire glycogen store. Fischler has established that some minimum of glycogen is essential for the liver cell to accomplish its manifold functions. If there is a lack of glycogen the liver cells become defenceless against

their own tryptic ferments, which otherwise serve in their protein metabolism and are digested themselves by their own proteolytic ferments. Thus results the picture of the central necrosis of the lobules. Applying these findings to our cases, we may understand why the extensive cell necrosis appears only in the later stages of mushroom poisoning. Through our findings we get an explanation for the peculiar clinical symptoms observed by all authors in the course of the fatal mushroom poisoning. If death does not occur in the first few days change for the worse may take place later and the patient die.

This aggravation shows itself in unconsciousness, convulsions or restlessness, symptoms which are known to be present clinically in acute yellow atrophy. Therefore, Treupel and Rehorn have assumed these symptoms to be the result of a disintegration of liver cells. Our histological findings make the clinical symptoms quite well understood; our conception of the alteration in the carbohydrate metabolism may give a hint as to the therapy, namely providing an abundance of sugar and avoiding protein. Treupel and Reborn have reached similar conclusions from a clinical standpoint, but the histological findings place their assumption on a better basis.

March 13, 1922.

REPORT OF A CASE OF ECHINOCOCCUS DISEASE OF THE KIDNEY*

HERMAN L. KRETSCHMER

Echinococcus disease of the kidney may be of two types: (1) The primary type, in which the kidney, as far as can be demonstrated clinically, is the only organ involved. This type of echinococcus infection is very rare. The case to be reported in this paper belonged to this type, as far as it was possible to determine at the operation. (2) It may be part and parcel of a general

* This paper will be published in detail in Surgery, Gynecology and Obstetrics.

infection in which this condition is found in other organs, such as the liver, spleen, intestinal tract, peritoneum, etc.

It is generally believed that renal hydatid is one of the rare kidney lesions even in countries where echinococcus disease is of common occurrence. In this country, where this condition is uncommon, there is a correspondingly small literature dealing with this subject. Lyon, in 1902, was able to collect a series of only 241 cases of echinococcus disease that were reported in the United States and Canada. Naturally the literature of renal hydatid would likewise be a small one. In the literature at my command I have been able to find seventeen cases reported, in which there was kidney involvement by echinococcus. This with the case to be reported below brings the total number of kidney cases reported in Canada and the United States up to eighteen.

G. Y., male, Greek, aged 32. Referred by Dr. George Parker, Peoria, Ill.

Past History.—In 1917, according to the patient's statement, he had an ulcer of the stomach, and influenza in 1918. Venereal disease denied.

Patient was cystoscoped three times in May, 1921, and tumor of the right kidney was diagnosed.

President Complaint.—When patient entered the Presbyterian Hospital he complained of pain over the right kidney region, frequency of urination, painful urination, hematuria and loss of weight.

Symptoms began one year ago with an attack of hematuria which lasted two weeks. At that time had an attack of severe pain over the right kidney region, lasting two hours, which radiated to the groin and back. Morphin was required for relief. Two days after the attack a "small round body about the size of a pea passed" which the patient described as soft with tiny particles of gravel in it. When allowed to dry it was crumbly and the particles had the appearance of gravel. Nothing was passed in the urine since that time. About two weeks after the first attack of hematuria he had a second attack which occurred without colic. This lasted about a week. No hematuria noticed since that time.

Pain over the right kidney began with hematuria. Has had ten or twelve attacks during the last year, lasting for a few

days each time. Pain is described as a dull ache along the twelfth rib, extending around in front to the level of posterior axillary line.

Frequency of urination is slight, but has been present at times. He has lost about 2 pounds in two months. Examination of abdomen showed no tenderness, rigidity or tumor masses. Kidneys were not palpable and not tender to fist percussion. Cystoscopy showed bladder negative. Ureters were catheterized without difficulty or obstruction. Phenolsulphonephthalein test was made and the dye appeared in 6.5 minutes on the right side and six minutes on the left.

Cell count and cultures from the urine showed the following:

	Cells	Cultures	Urea
Bladder	30	Sterile	.013
Right kidney	50	Sterile	.008
Left kidney	30	Sterile	.018

Roentgen-Ray Examination.—At a point near the upper pole of the right kidney there is a shadow which is apparently the lower margin of a mass the envelop of which is calcareous in nature. This curved calcareous line when followed outward and upward is incomplete, so that only part of the envelop is calcareous. The presence of this area of calcification was demonstrated in the specimen removed at operation.

Pyelogram.—The upper calyx is deflected inward and the middle calyx deflected downward at a point where the calcareous mass impinges upon the pelvis.

Operation, June 28, 1921. Right kidney exposed by the usual oblique lumbar incision. Perirenal fat dissected away, exposing a large, firm globular mass about 20 cm. in diameter, occupying the upper half of the kidney and bound by firm fibrous adhesions to the surrounding structures. Kidney pedicle was clamped, doubly ligated and clamps removed. Ureter was secured and ligated about 10 cm. distal to pelvis, and kidney removed. During the operation a very large hole was torn in the peritoneum, because of the difficulty in delivering the tumor and because of the presence of adhesions. This large opening gave an excellent opportunity to examine other organs before closing the wound. The liver was very carefully gone over for the presence of echinococcus cysts, but apparently it was normal. Exploration of the rest of the abdomen was negative.

The patient had a rather stormy convalescence for about ten days and complained of a great deal of abdominal pain, nausea and vomiting. At one time 300 c.c. of fluid were obtained from his stomach and a provisional diagnosis of acute gastric dilatation was made. After his gastric symptoms had subsided, patient made an uneventful recovery.

Gross Description of the Kidney: The kidney measured 13 cm. in length, 7 cm. in width and 5.5 cm. in thickness. In the upper, outer half was a tumor 11 cm. long by 11.5 cm. in width and 8.5 cm. in thickness. The tumor projected from the upper half of the outer convex border and extended obliquely downward toward the lower pole so that the lower border was 7 cm. above the latter point. Exteriorly, the mass was firm and smooth except for very slight roughening, caused apparently by bundles of fibrous tissue, and the color was pink to yellow white. When opened the tumor proved to be a sac with a firm fibrous wall about 1 mm. thick, smooth and yellow inside, and from which a cheesy yellow material could be scraped in small quantities. The inside of this tumor was filled with many small cysts, in size from a few millimeters in diameter to 10 by 6 by 2 cm. Some of them were filled with clear fluid; others were empty and several layers thick, the walls composed of gelatin-like material, rolled up like a scroll in some instances. Quite a number were free in the sac and were filled with a clear colorless fluid which could be seen through the wall of the cysts, which was almost transparent.

Two echinococcus fixation tests were made with the following results: April 24, 1922, negative, complete hemolysis with human cyst fluid, positive, 75 per cent. inhibition of hemolysis with pig cyst fluid; June 7, 1922, negative, with human cyst fluid, positive, 25 per cent. inhibition of hemolysis with pig cyst fluid.

Feb. 13, 1922.

HYDROGEN ION CHANGES WITH THE AGGLUTINATION OF BACTERIA BY IMMUNE SERUM *

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The medium in which bacteria are agglutinated by homologous immune serum increases in alkalinity in proportion with the completeness of the agglutination. The curve representing this change in a series of immune serum dilutions resembles closely a titration or dissociation curve. When bacteria are suspended in

* A complete report will be published in the Journal of Infectious Diseases.

normal salt solution, they behave chemically and electrically like the anion of the salt of a strong base and a weak acid. The change in the reaction of the medium with the agglutination of bacteria by immune serum is believed to result from the liberation of base (Na) during the reaction.

April 10, 1922.

PERSISTENT PATENCY OF THE DUCTUS ARTERIOSUS BOTALLI

H. GIDEON WELLS

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In 1907 I reported before this society a case of persistent patency of the ductus arteriosus, and at that time was able to collect from the literature reports of forty-one well authenticated cases [1] of such persistency unaccompanied by other cardiovascular defects to which persistent patency is often secondary. In 1915 Stoddard [2] was able to collect but twenty-two cases reported since my paper, and of these only five were in patients over 1 year of age. All told, there seem to be in the literature but about twenty-five cases of uncomplicated persistent patency of the ductus in adults. In view of the evident infrequency of this condition a second case which I have observed is herewith placed on record.

The subject was a laborer, born in Germany, 50 years old, who was brought into the Cook County Hospital on May 27, 1918, having been found sitting in the corner of a street car, unable to speak, and with the right half of the body paralyzed. Although there was nearly complete motor aphasia he could hear and understand questions, and it was learned that he had been entirely well up to the time of this sudden paralysis. He had had no serious illnesses previously, denied venereal infections, and indicated that he had had no cardiac or respiratory symptoms. Examination revealed complete right-sided hemiplegia, with the usual physical findings, the spinal fluid containing no blood but with a slight increase

1. Amer. Jour. Med. Sci., Sept., 1908. This article contains the full details of my first case and a review of the literature.
2. Arch. Int. Med., **16**: 38, 1915.

in protein content and under somewhat increased pressure. The Wassermann reaction was negative, on both the blood and the spinal fluid. Examination of the heart disclosed no abnormalities whatever except a soft mitral murmur, which was not transmitted. The blood pressure was 150-100. He developed a hypostatic bronchopneumonia from which he died on June 5, and the postmortem examination was made on June 8. This revealed extensive hemorrhage into the basal ganglia on the left side, apparently secondary to an extensive thrombosis and arteritis of the small arteries of this part of the brain. There was also an extensive hypostatic bronchopneumonia in the right lung. There were no other findings of importance outside the heart and vessels, which were described as follows:

The heart is very broad transversely, and the apex is round and flat. The ventricles are distended. The coronaries are neither beaded nor calcified. There is a patent ductus arteriosus opening into the aorta which can be followed down with a probe into the pulmonary artery. Over the opening into the pulmonary artery, there is a fold of pulmonary membrane, which is soft and protrudes 1 to 2 mm. into the artery. The opening into the pulmonary artery is at the summit of this mound, being between 1 and 2 mm. in diameter. The ductus is cone-shaped, its apex being in the mound-like protrusion into the pulmonary artery, the main part of the duct being about 5 mm. in diameter, but widening out to 1 cm. diameter at its opening into the aorta. Its walls are thick, like the aorta, and it shows a slight diffuse sclerosis, most marked at the aortic orifice, but without atheroma or thrombosis. There is no evidence of inflammatory changes about the ductus. The pulmonary artery shows no sclerosis, stenosis or other abnormalities. The aortic and pulmonic valves are normal. There is no opening between the ventricles. The foramen ovale is open, the opening being slit-like and about 1 cm. long. There is a fold of endocardium over this opening and so it is not functionally patent. The right ventricle is normal in thickness, the left is 12 to 15 mm. thick. The muscle is extremely flabby, but there is no fibrosis. The weight is 400 gm.

The thoracic aorta is slightly sclerosed in the lower portion.

The large vessels are free from thrombi. The veins of the pia arachnoid are very much engorged. The arteries at the base of the brain are thin and pliable, and free from any signs of sclerosis. All of the large vessels of the brain are free from sclerosis and no thrombi can be found in the main branches.

Despite the fact that the ductus had been sufficiently patent to prevent its normal involution through sclerosis, evidently this had been without any considerable effect on the circulation as attested by the lack of any hypertrophy of the right ventricle. The amount of circulation through the ductus had not been sufficient to cause a murmur noticeable on examination of the chest. There were no clinical features to direct particular attention to the heart, so that nothing more than the usual routine examination was made; therefore we do not know whether there were any manifestations that might have been detected by more intensive study.

In all respects this case is typical of the usual findings in uncomplicated cases of patent ductus arteriosus reaching mature years without noticeable clinical effects, the patent ductus being conical with its wide end at the aorta, and the pulmonic opening situated on a mound of raised intima.

April 10, 1922.

FUSIFORM BACILLI AND SPIROCHETES IN PREPUTIAL SECRETIONS

J. BRAMS AND I. PILOT

The bacteriology of cases of erosive and gangrenous balanitis was studied and fusiform bacilli together with spirochetes were found constantly in large numbers. Associated with these organisms were varying numbers of other bacteria chiefly of the staphylococcus group. Saliva contact has been stated by many observers to be factor in introducing the infection. The absence of a history of saliva contact in these cases led to an investigation of the bacterial flora of the normal preputial secretions of a hundred individuals. From these studies the following conclusions were made.

1. Under normal conditions fusiform bacilli together with spirochetes were found in the preputial secretions of 51 per cent. of 100 individuals.

2. Associated with these organisms were staphylococci, and occasionally colon bacilli, streptococcus hemolyticus and viridans and diphtheroids.

3. A comparative study of the flora of the normal perputial secretions and the secretions and pus from cases of balantitis revealed a striking similarity in both smears and cultures.

4. Special interest centers about the fact that with fusiform bacilli and spirochetes normally present in the preputial sac balanitis is not dependant upon the introduction of these organisms through saliva contact but may arise locally particularly in individuals with retention of secretions and phimosis.

April 10, 1922.

SPORO-AGGLUTINATION IN THE DIAGNOSIS OF SPOROTRICHOSIS

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From the Department of Pathology and Bacteriology, University of Illinois, College of Medicine, Chicago

In sporotrichosis not infrequently cultures made from lesions remain negative. This is true especially in cases of long duration and in patients who may have been treated with potassium iodide. It is in such instances that sporo-agglutination is applicable as a diagnostic measure.

The present status of agglutination in this disease based on the work of a number of men is approximately as follows:

Normal human serum agglutinates the spores of this organism in dilutions varying from zero to forty. Many sera are negative even when undiluted. The serum from cases of sporotrichosis gives positive agglutination in dilutions varying roughly from 300 to 1,500. Serum from cases of various mycoses occupies an intermediate stage in that there may occur a group agglutination of from 40 to 150. An instance is recorded of an agglutination of 1-400 in a case of hemisporosis. The mycoses include actinomycoses, blastomycoses, hemisporosis, etc.

The technique of the sporo-agglutination test briefly is as follows: A culture of the sporotricha two to four

weeks old is shaken down in salt solution, then centrifugated thus separating the spores from the mycelium, the former remaining in suspension. Dilute so as to obtain several hundred spores in a microscopic field. This is then mixed with the serum in increasing dilutions and readings being taken in twenty-four hours. The microscopic method should be used.

A woman (patient at Cook County Hospital), aged 47, developed a typical sporotrichotic lesion on the finger with ascending subcutaneous nodules of the arm following a puncture wound at the same site received while preparing a rabbit. After three months she entered the hospital and a clinical diagnosis of sporotrichosis was made by Stillians and others. The primary wound had largely healed and cultures from it as well as from small abscesses on the arm yielded negative results for sporotricha. Her serum agglutinated a known culture of sporothrix at a dilution of 1-640, thus confirming the clinical diagnosis. Two other cases with negative cultures in which a diagnosis of sporotrichosis was considered clinically, though the lesions were not typical, yielded slight agglutination at dilutions of 1-40. On this basis we felt justified in ruling out a sporothrix lesion. Later events proved these decisions correct. We suggest the application of this method in all cases where the evidence is at all suspicious of sporotrichosis.

April 10, 1922.

SEROLOGIC OBSERVATIONS ON GONORRHEAL ARTHRITIS

RUSSELL D. HERROLD

The literature on the use of autoserum therapy in various disease conditions was reviewed.

An analysis was made of the precipitin and complement fixation reaction with the joint fluids and blood serums of ten patients with gonorrheal arthritis.

It was found that the blood serums as a rule contained a greater amount of complement binding substances than the joint fluid of the same patient.

Precipitin tests with antigonococcus horse serum and joint fluids gave positive results in dilution from 1-800 to 1-2,400. The antigen control of normal joint fluid, idiopathic hydrocele fluid and extract of purulent exudate did not give a precipitate in a higher dilution than 1-200. These nonspecific proteins were absorbed by treatment of the antigonococcus serum with 1-200 dilution of normal human serum while the joint fluids remained positive. It would seem therefore that gonorrheal joint fluids contain sufficient gonococcus precipitinogen to differentiate the condition from other causes of fluids in joints.

Polyvalent antigonococcus horse serum was given intra-articularly in four cases after aspiration of the synovial fluid and irrigation of the joint cavities with normal salt solution. Favorable results were obtained.

May 8, 1922.

A CASE OF MAMMARY ADENOCARCINOMA WITH PECULIAR RELATION TO THE GLANDS OF INTERNAL SECRETION

From the Department of Pathology, Loyola University School of Medicine

PAUL KLEMPERER

Since the first report of Erdheim, the relation of the parathyroid gland to the calcium metabolism is well known. Erdheim's anatomical findings of parathyroid hyperplasia in osteomalacia were confirmed by several authors and extended to other conditions of bone destruction as osteitis fibrosa and osteoporosis. The extensive bone destruction in generalized bone carcinomatosis has not as yet been taken into consideration.

A case of mammary cancer with an extremely involved skeleton occasioned an examination of the parathyroid bodies. Three of these were found normal in size and shape, the left inferior body was replaced by a tumor measuring 30 by 5 by 3 mm., entirely separated from the thyroid gland. The histological examination

revealed a tumor composed of both kinds of parathyroid cells, chief and eosinophile cells. The former were arranged mostly as cords, partly, however, as alveoli. The latter were accumulated in relatively large groups and islets, one group harboring a small cancer metastasis. The fact that the tumor was composed equally of both kinds of the normal parathyroid gland suggested its conception as a hyperplasia, not as a true tumor. Therefore, we are entitled to bring it in relation to the bone destruction.

Regarding the question whether the hyperplasia is the cause or the result of the bone destruction, there is no doubt that it is due to the cancer metastasis in our case. This fact would seem to support the assumption of most writers, that the hyperplasia of the parathyroid gland in bone destruction is to be considered as an increased functional activity tending to compensate for a disturbed calcium metabolism. Yet the fact that we could not find any trace of calcification in newly formed osteoid tissue is against the conception that hyperplasia indicates a hyperfunction. The histology of a really hyperfunctioning parathyroid gland is not definitely known. Tomaszewski described these glands in cases of abnormal calcium deposition in the body as in calcified ribs, atherosclerosis and calcified tuberculosis as hyperfunctioning glands. But inasmuch as these calcium depositions are not very extensive and occur mostly in older persons, accompanied by more or less extensive osteoporosis, these observations seem to furnish no definite evidence. However, in all cases of bone cancer, particularly in the extensive osteoplastic forms of prostatic and mammary cancer, we have to do with a condition of an entirely changed calcium metabolism involving both a calcium destruction and an accumulation to a very high degree. A careful examination in such cases could undoubtedly throw some light upon this obscure field of internal secretion.

Further, we found a metastasis in the pituitary gland which destroyed almost the entire posterior lobe but did not involve the glandular part. The fact that a complete destruction of the posterior lobe did not increase

the urinary secretion corroborates the results of Leschke, that the nervous part of the pituitary gland does not regulate the urine secretion.

May 8, 1922.

A CASE OF LIPOMA OF THE SIGMOID

SIDNEY A. PORTIS

In 1904 Ward reported a case of lipoma in which tumor was passed by the rectum after a long period of constipation. There was much gastric disturbance and abdominal pain. Rooney later reported seven cases of lipoma of the large intestine in which many if not all of the tumors were expelled spontaneously through the rectum. Dewes [3] in 1906 reported eighteen cases in all, seven of the caecum and ascending colon, five of the sigmoid and six of the rectum. Kellert [1] in a review of the literature from 1906 to 1917 says that nineteen cases of lipoma had been reported, four of the caecum and the rest of the remaining portion of the colon. He reports an additional case and summarizes the symptoms as chronic constipation, vague abdominal pain, frequent attacks of severe pain and finally symptoms of intestinal obstruction. Ewing [2] states that gastro-intestinal lipomas are rare and that they arise from submucosa and appendices epiploicae of the colon. Kathny [5] reported a case in 1920 in which patient experienced a sudden sharp pain in the abdomen which would occur irregularly and would be relieved by bowel movement. Carlueci [4] in 1921 reported two cases seen by himself in which the main symptom was recurrent abdominal pain relieved by bowel movement. The Bellevue Hospital records [6] from 1911 to 1920 show one case of intussusception due to lipoma in 120 cases of intestinal obstruction; of the 601 benign tumors, eighty-five were lipomas, but more of them were intra-abdominal.

Case report: Mrs. B., seen on March 2, 1921, complaining of cramp-like pains in the abdomen, diarrhea and loss of weight. Up to two months before, she had been apparently well. Since then, there have been cramp-like pains in the

abdomen with rumbling and gurgling and desire for bowel movement, the latter relieving the distress. This distress may last from one to three hours at a time and is more noticeable after a heavy meal. Movements are watery at times, with much mucus and blood but no pus. No nausea, vomiting nor belching; afraid to eat because of the distress and quite nervous, easily excited. Has palpitation, no cough nor night sweats; no headaches but some vertigo. Has lost 10 pounds in weight since onset and is much weaker. She has two children living and well; one induced miscarriage at the end of six weeks. Father died of carcinoma of the rectum. No history of tuberculosis in the family. Menstrual periods began at 12, three-day duration, twenty-eight-day type. She had the usual diseases of childhood, also typhoid fever, sore throat, and has had some vaginal repair of the uterus. She is active, sleeps well, drinks one cup of coffee and one cup of tea a day and does not indulge in alcoholics.

Physical examination showed a rather obese white woman of about 40 years who did not look acutely ill. Temperature 98.4, pulse 88 and weight 182½ pounds. Thyroid not palpable, fine tremor of the hands and tongue; reflexes intact. Eyes reacted normally to the usual muscle tests; no demonstrable glandular enlargement. Lungs normal; heart normal; blood pressure 128 and 70. There was marked tenderness in the region of the sigmoid and an indefinite mass was felt here; also tenderness over the gallbladder. Rectal examination with proctoscope revealed no evidence of stricture or tumor, but bowel was hyperemic and high up was seen a large amount of thick green-yellow mucus. The urine contained a slight amount of albumin, some indican and microscopically there was one red cell to a high power field. The stool was liquid, contained a large amount of mucus; positive Weber test. There was some fat, starch and undigested muscle fibre, also pus cells. The stomach acids were 55 free and 65 total on the motor meal and no evidence of retention. The Ewald meal showed 30 and 65 and normal digestion of pepsin. Hemoglobin, 85; reds, 4,450,000; whites, 14,500; small mononuclears, 23; large mononuclears, 4, and 73 polymorphonuclears; 2 transitionals. Wassermann test negative.

The roentgen ray revealed a substernal shadow resembling a subthyroid. The lungs and heart were negative; the stomach and duodenal bulb also negative. No bismuth seen in the descending colon at the twelfth hour. Twenty-fourth hour showed bismuth massed at sigmoid, also the forty-eighth hour.

Barium enema: Barium enters rectum without any apparent obstruction. It goes into the first portion of the sigmoid

where it meets with an apparent obstruction and it seems to envelop a large mass. The bowel is highly spastic here. There is a marked redundancy of the bowel just above this spasm; bowel is quite large from hepatic flexure to the splenic flexure which is held high up. There is marked tenderness in the region of the spastic sigmoid. There are no other defects in the bowel above this point.

Patient began to lose weight and although advised surgical intervention, she refused operation. March 28, she said she had a severe cramp-like pain in the lower abdomen with desire for bowel movement, but without success. She then took an enema and passed a large mass which is described by Dr. A. M. Moody as follows:

"A tumor mass, 7.5 cm. x 5 cm. x 4.5 cm., gangrenous and one half covered by intestinal mucosa, the other portion is necrotic and ulcerating. The mass is foul smelling. It is roughly pear-shaded with a narrow pedicle by which it was undoubtedly attached to the bowel.

Sections of the margin of the tumor consist of necrotic mucosa and submucosa and muscularis with lobulated fatty tissue beneath. The bulk of the tumor is fatty tissue with fibrous trabeculae. The blood vessels are abundant and filled with blood. In many regions blood has escaped into the tissue. The entire mass is infiltrated with polynuclear leucocytes.

Diagnosis: Pedunculated lipoma with strangulation, secondary infection and gangrene."

Since passing the tumor, the patient has been comfortable and free from symptoms.

Of the various cases reported in literature, the history is usually that of chronic constipation, vague abdominal pain, frequent attacks of severe pain relieved by bowel movement, especially that through enema, and finally symptoms of obstruction may occur. The findings are those usually of tenderness in the region of the tumor. There may or may not be a palpable tumor mass. The final abatement of the symptoms after a passage of the tumor or a surgical removal of it seems to be the general result of all the cases reported in literature.

May 8, 1922.

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SACROCOCCYGEAL CHARDOMA*

EDWIN F. HIRSCH
AND
MARY INGALS

From the Pathological Laboratory of St. Luke's Hospital, Chicago

This tumor was removed surgically from the posterior surface of the sacrum. It is 9 by 9 by 3.5 cm. and histologically contains vacuolated epithelial cells undergoing mucoid degeneration, the appearance corresponding to the descriptions of chardomas. There is no recurrence eighteen months after removal.

May 8, 1922.

GUMMAS OF THE BASE OF THE HEART WITH SYPHILIS OF THE AORTA

NEWTON MILLER

From the Pathological Laboratory of Rush Medical College

This heart was taken from a man found dead in bed. An autopsy was performed because there was no evident cause for death and because the man had complained of sustaining a fall on the day of his death in a lumber yard where he was employed. He had returned from his work, refused his evening meal and had gone to bed at 7:30 p. m. One-half hour later his wife found him dead.

Necropsy (Dr. E. R. LeCount): The body was that of a man 50 years old, well nourished and with no external injury. There was a scar on the dorsum of the penis. The abdominal viscera were without noteworthy change; the abdominal periaortic lymph glands, small, yellow and firm; hypostatic pulmonary edema; no tuberculosis of the lungs or tracheobronchial lymph glands. The pericardial fluid was straw-yellow and clear. The two layers of the sac ventral to the aorta, adherent 3 cm. more caudad than usual.

Further study revealed the following: The heart with the aorta weighs 680 gm. The epicardium is everywhere smooth

* A complete report will be made in the Journal of the American Medical Association.

and shining. A layer of fat is along each coronary artery and about the base of the heart; that along the anterior coronary is 6 mm. thick at the base of the vessel. Both ventricles extend to the apex of the heart. The wall of the right ventricle is 8 mm. thick, the left 22. The posterior cusp of the mitral valve is thickened and opaque with a yellowish white sclerosis. The semilunar cusps of the aorta are also thickened but not stiffened. The tricuspid leaflets are all yellowish white, thickened and opaque. There are no changes of the pulmonary leaflets. At the orifice of the pulmonary artery a thickened endocardium begins and extends into the ventricle 4 cm. before it thins out to normal. There is a median strip of the anterior wall 1 cm. wide which is not affected. Yellowish masses 5 to 12 mm. in diameter are seen and easily palpated in the right ventricular wall at the base of the ventricle and along its septal margin and dissection uncovers a layer of connective tissue 5 to 8 mm. thick immediately beneath the thickened ventricular lining. Within this layer are located the yellowish necrotic masses mentioned and many more smaller ones 2 to 4 mm. in diameter, with others which are irregular, flattened, and 2 to 5 mm. thick. There is so much overlapping and fusing of masses that the thickened endocardium is underlaid almost at every point with necrotic material. The largest yellowish body is 12 mm. in diameter and has a jelly-like center 4 mm. in diameter, a little softer than the yellow substance. The connective tissue is concentrically arranged about some of the masses but not about others. These gummas with their connective tissue capsules are 4 to 25 mm. in diameter; one 25 mm. long and 15 wide is in the wall of the right auricle above the septal leaflet of the tricuspid valve. Another, slightly raised and reddish, 12 by 18 mm. is in the wall of the pulmonary artery 5 mm. distal to the left cusp.

In the lining of the coronary arteries are yellowish-white irregular patches 2 to 4 mm. long and slightly raised. This condition involves the proximal 5 cm. of each artery. The circumflex branch of the left coronary is slightly thrombosed.

The aorta is 2 mm. thick and 10 cm. in circumference, 5 cm. distal to the leaflets; 7 cm. in circumference, 5 cm. distal to the left subclavian artery and 4.5 cm. at the mouth of the superior mesenteric artery. The first 15 cm. of the lining is everywhere roughened by raised areas, 1 to 2 mm. high, 5 to 25 mm. across. Raised striae are here and there interposed among the patches. The raised patches are in the media,

indurated and yellowish-white or pinkish. Distal to the arch, the elevated areas become less numerous. There are three small aneurysms in the aortic wall above the right cusp of the semilunar valve. The orifice of the first, 7 by 10 mm. is 1 cm. distal to the cusp. The pouch is flask-shaped, 15 mm. deep and 18 in diameter. The orifice of the second, 8 by 11 mm. is 18 mm. distal to the cusp. The sac is 14 mm. deep and flares out like a flask with a diameter of 22 mm. Its proximal side is in contact with the anterior coronary artery. These two sacs are proximal to the transverse sinus and bulge into the left auricle to which they are closely adherent. The orifice of the third, 6 by 5 mm. is 4 cm. distal to the leaflet. It is more tubular than the other two, has a depth of 12 mm. and is distal to the transverse sinus. The lining of the aorta is extended to line these aneurysms. There is a layer of fibrin 1 mm. thick in each sac. There are no changes in the pulmonary artery except as noted.

Histology: In sections from the anterior wall of the base of the right ventricle, there is a circular, necrotic mass 5 mm. in diameter, 2 mm. from the endocardium. The outer fourth of this region is dotted with fragments of nuclei which increase in size and number towards the periphery. At the periphery are nuclei and cells in all stages of degeneration mingled with fragments of connective tissue. Around this is a zone 0.2 mm. wide composed of round cells and a few plasma cells infiltrating a connective tissue matrix. A second outer zone is connective tissue 1 to 2 mm. thick, replacing the heart muscle with exception of a few isolated groups of muscle cells in various stages of degeneration. There are multiple foci of round-cell infiltration in this outer zone, in the fatty areolar tissue beneath the epicardium and in the epicardium itself. In spite of careful search, no giant cells are found in any of the sections, and in suitably stained sections no tubercle bacilli can be demonstrated. The arteries are partially or completely closed by obliterating endarteritis.

With a total absence of demonstrable tuberculous lesions anywhere in the body, and the condition described, the following diagnosis is made: Gummas of the right ventricle, auricle and pulmonary artery; syphilitic aortitis; multiple saccular aneurysms of the aorta; sclerosis of the coronary arteries; partial thrombosis of the circumflex branch of the left coronary artery; obliterating endarteritis of the small cardiac arteries; hypertrophy of the wall of the left ventricle.

May 8, 1922.

A CASE OF MENINGEAL ENDITHELIOMA SIMULATING A TUMOR OF THE HYPOPHYSIS

BERNARD PORTIS

The case I wish to report is a meningeal endothelioma arising from the capsule of the pituitary body, and simulating very closely a tumor of the hypophysis proper. This case is reported because of the unusual site of origin, and because death was apparently due to a hemorrhage caused by the tumor and infiltrating diffusely the leptomeninges, a rather rare occurrence for this type of tumor.

The capsule of the pituitary body is a derivative of the dura (Cushing) and is continuous with the dural diaphragm over the sella turcica, hence, a dural origin of this tumor would seem obvious.

Ewing in his text on Neoplastic Diseases describes two varieties of meningeal endothelioma—one a perivascular tumor and the other the psammoma. This latter is in reality only the result of retrogressive changes in the former, such as hyalinization and calcification. These tumors may be single or multiple, small or of considerable size and usually arise from the inner side of the dura. Their growth is slowly progressive, causing a corresponding displacement or atrophy of the adjacent tissue. The chief sites of origin are from the dura over the convexity, falx and tentorium. Their structure histologically is very characteristic, and the endothelial features are obvious. The tissue is composed of systems of cells, concentrically arranged about a central lumen, closed or patent, representing a rudimentary vessel, and resembling very closely the epithelial perles of a squamous cell carcinoma. The cells are usually polyhedral, or elongated spindle cells. These accumulations of cells frequently show hyaline changes. The origin of these tumors has generally been ascribed to the endothelium of the perivascular lymphatics, or to the perithelium of the proliferating vessels, but Kaufmann considers the possibility of their connective tissue origin.

Mallory has confirmed this conclusion of Kaufmann in a careful study of thirty tumors of the so-called dural endothelioma type. He states that there is no dural endothelioma, but merely the presence of fibroblasts lining it. By means of four differential stains he clearly demonstrated that these tumors arise from connective tissue. He furthermore concludes that these tumors should be called arachnoid fibroblastoma, because they originate from the outer undifferentiated layer, which is potentially fibroblasts.

The following report includes the clinical findings, and the autopsy findings of Dr. H. G. Wells.

Clinical History.—The patient was a housewife, aged 50, who entered the hospital on Jan. 8, 1922, at 1:30 a. m., in a comatose condition. The history was obtained from her husband, who said that for the last eight days the patient has not been feeling very well, complaining of more frequent frontal headaches. These, however, were not associated with vomiting, and caused no alarming symptoms.

Today, Jan. 7, 1922, the patient ate her usual dinner at about 1:30 p. m. with her husband; she then went about her work scrubbing the floors. Her husband left the house and returned about 8:30 p. m. When he entered the house he found the mop and pail in the middle of the room. He went to the lavatory, and there found considerable vomitus all over the floor. His wife was lying on the bed in a prostrated condition, and complained of severe frontal headache. The husband procured two headache powders which he then gave to her, but without any abatement of the symptoms. She then became delirious and had a slight convulsion before entering into deep coma. A doctor was called and he sent her to the Illinois Central Hospital.

Past History.—The patient has complained of severe frontal headaches since early childhood, but these were never accompanied by the migraine symptom complex nor any definite cerebral symptoms. The dimness of vision was apparently due to presbyopia. A panhysterectomy had been performed on June 26, 1916, for fibroids, ovarian cyst and bilateral salpingitis. She had been married eleven years, and was never pregnant. Family history is essentially negative.

Physical Findings.—The patient is an obese woman about 50 years old, who is severely ill and in a state of coma. Involuntaries are present. There is no evidence of trauma, nor discharge of blood from the ears and nose.

The patient became progressively worse, coma increasing and she died within three hours after entering the hospital.

AUTOPSY

Anatomical Diagnosis. — Endothelioma of the meninges extending over the hypophysis with pressure enlargement of the sella turcica, extensive hemorrhage into the leptomeninges at the base of the brain, slight dilatation of the left internal carotid artery, slight hypertrophy of the heart, slight arteriosclerotic atrophy of the kidneys, especially of the left kidney, with cyst formation, obliterative fibrous pleuritis with healed calcified tubercle in left apical pleura, passive congestion and fatty changes in the liver, operative removal of the uterus, ovaries and tubes with healed laparotomy scar, obesity, healed gastric ulcer, postmortem digestion of pancreatic fat tissue.

The calvarium was normal. The dura mater was under noticeable tension, and the veins of the cortex were distended. Over the left temporal region was a diffuse infiltration of blood beneath the pia-arachnoid, and a smaller amount over the right temporal region. There were no adhesions between the dura and pia-arachnoid. Between the optic nerves and in front of the optic chiasma, a tumor was found, and around this tumor mass was considerable hemorrhage. The ventral surface of the brain was covered by a diffuse clot of very dark blood, symmetrically disposed in the pia-arachnoid from the tip of the frontal lobes into the spinal canal, forming a uniform sheet of blood. Laterally it extended as far as the Sylvian fissure on either side, more on the left than on the right. The hemorrhage also appears between the lateral hemispheres. Both the right and left lateral ventricles contain a blood stained fluid and a small amount of clot. The basal ganglia were free from hemorrhage. The largest amount of blood was found over the cystic chiasma.

Protruding between the optic nerves was found a rounded fleshy mass 13 mm. across in the presenting aspect, surrounded by a blood clot. The sella turcica was distinctly enlarged measuring 20 mm. in its transverse plane and 16 mm. in its anteroposterior plane. This mass was so located that it seemed to be a typical anterior lobe hypophyseal tumor.

On section it showed two distinct portions, a deep red posterior mass corresponding in shape, size and location to the normal hypophysis, and an anterior pale pinkish tumor mass about 12 mm. by 12 mm., with a small mass of similar

material around the infundibulum. The anterior part of the tumor has grown forward on the anterior surface of the sella turcica, which is distinctly broadened and flattened by pressure, but not eroded or invaded. The optic nerves are not noticeably compressed.

The remainder of the usual routine autopsy was performed and the findings are recorded in the anatomical diagnosis given above. The histology of the tumor revealed a tissue resembling the typical meningeal endothelioma already described, with some hyaline changes but little tendency to psammoma formation.

May 8, 1922.

SPECIMENS FROM A CASE OF XANTHOMA TUBEROSUM MULTIPLEX

B. BARKER BEESON

These specimens were taken from a case seen by me at the House of Correction. The gross specimen was removed from the extensor surface of the patient's left elbow, through the courtesy of Dr. W. H. Hazlett. Similar growths were present over the other elbow, the knees, the Achilles tendons, the hands and along the outer aspect of the left arm. All of them were saffron colored, soft, indolent, sharply defined and elevated from one to three inches above the surrounding integument. Those about the knees and elbows were larger and distinctly pedunculated. The tumor shown measured four by two inches, being slightly smaller than the growths about the knees.

Histologically, the normal elements of the derma had been more or less replaced by a new formation composed of numerous, large connective-tissue-like cells which stained an intense orange red with Sudan III. These elements, some of them veritable giant cells, formed sharply defined perivascular nodules which were separated from one another by bands of newly formed connective tissue. The fatty substance or lipochrome is present in these cells in the form of droplets. Counterstaining with hematoxylin makes the picture a better one. The epidermis showed only a very

slight reaction to the Sudan III, practically all of the new growth being below the level of the papillary layer.

Dr. P. G. Albrecht of the Department of Physiologic Chemistry, College of Medicine, University of Illinois, very kindly performed several chemical examinations of the blood with the following results. In each case the figure stated is the amount in 100 grams of blood. For purposes of comparison the normal figures as stated in Hawk's Manual are also given.

	Normal	In This Case
Cholesterol	140 to 180 mgm.	182, once 222, second time
Nonprotein N.	25 to 35 mgm.	26.3 mgm.
Preformed creatinin	0.7 to 1.3 mgm.	1.62 mgm.
Sugar	0.08 to 0.11%	0.14%
Fat	0.10 to 0.7%	0.80%

Thus the cholesterol was increased, although not so much as has been noted by other investigators. Chauffard has found 600 mgm. of that substance in 100 gm. of blood in such cases. Schmidt, in five examples of this curious disorder, reported that the cholesterol varied from 259 to 572 mgm. per 100 gm. of blood.

The patient, a man, aged 34 years had had these tumors ever since he could remember. Several surgical removals had always been followed by recurrence in situ. Two brothers are said to have similar new growths. In addition my patient presented a mitral and aortic regurgitation. The usual laboratory tests revealed nothing of special interest. No bile was found in the urine and there was no history of jaundice. An X-ray plate of the heart showed no pericardial involvement.

May 8, 1922.

TRANSACTIONS OF THE
CHICAGO PATHOLOGICAL SOCIETY

VOL. XI. FEBRUARY 1, 1923. NO. 8

A PLEA FOR THE DEVELOPMENT OF PATHOLOGY *

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Pathology, in its early development, was a by-product of anatomy during that period when the first dissections of the human body were developing anatomic knowledge. Morgagni, Vesalius, Fallopius, Eustachius, and others of the earlier anatomists, whose names are still attached to hydatids, tubes and various other structures of the body, made note of abnormalities encountered in the course of their anatomic investigations. Pathology, during this early stage of its development, could not be considered a subdivision of knowledge with standing of its own. It noted objectively gross anatomic deviations from the normal, but, because of the fantastic humoral doctrines of disease then prevailing, it could not intelligently concern itself with the processes that had led to the abnormalities.

It was not until Virchow showed that the cell doctrine applies to abnormal tissues as well as to normal ones that pathology began to establish itself as the most fundamental of the medical sciences. With the knowledge that the constituents and products of abnormal tissues are derived from preexisting normal structures, it became possible to establish the fact that abnormality

* President's address, read before the Chicago Pathological Society, Oct. 9, 1922.

* From the Nelson Morris Memorial Institute for Medical Research of the Michael Reese Hospital.

is not some new and distinct state of the body, for the explanation of whose causation it was necessary to suppose mechanisms foreign to those usually at work. It became possible to show that pathologic lesions result from mechanisms of which the body normally makes use, and we began to arrive at an understanding of processes as opposed to anatomic end-results. It was quite a distinct advance in our conception of disease to know, for instance, that the pus corpuscle is a derivative of the normal leukocyte, axiomatic as such knowledge may seem to us today. But it was an even greater advance to learn that the mechanisms which lead to pus formation are physiologic ones which the body employs under normal conditions.

PRESENT STATE OF PATHOLOGY

With the applicability of the cell doctrine to abnormal tissues established, pathology entered on the era which has added to medical literature a long list of most illustrious names. The leaven added by Virchow and his successors is still at work, but it is fair to ask whether America has contributed and is contributing its proper share to the advancement of pathology. If we have not done and are not doing our share, then it behooves us to inquire into causes and to attempt to overcome the retarding forces that may be operative. Our first question we shall have to answer in the negative; we shall have to admit that this country has not contributed as much as it ought to the literature of pathologic anatomy and histology, and that, with only one or two exceptions, it has not developed any outstanding philosophers in the field of pathology. Unfortunate as this is from the standpoint of the development of pathology, it reflects itself even more seriously in the attitude of the large body of the medical profession, the clinicians and practitioners, toward pathology. It reflects itself also in the medical education of the country; the medical student is all too apt to look on pathology as one of the "theoretical" subjects of the first half of the curriculum, subjects which are to be forgotten as rapidly and as completely as possible during the final two years of "practical" work.

FACTORS THAT HINDER DEVELOPMENT

The factors that underlie the present state of pathology in this country are probably national, rather than local, in character. First and foremost in importance is the unsympathetic and even antagonistic attitude toward postmortem examination, an attitude manifested not only by a large part of the lay public but also, unfortunately, by a part of the medical profession. Medicine, in this country, has not yet achieved for itself such a position that every possible aid is given it as a science whose chief aim is the betterment of the condition of mankind. Too many pathies and cults share with scientific medicine the affections of the laity, for medicine to demand as a right certain privileges which it should have. The result is that the layman, even if he is of more than average intelligence, does not understand the importance of the necropsy to medicine, nor has he any appreciation of the effect which knowledge gained at the postmortem table may have on some ill to which he may later fall victim. A change in conditions, which would result in the performance of necropsies in a minimum of from 75 to 80 per cent. of all patients dying in hospitals, would evidence itself in a short time by an incalculable development of pathology, of medical teaching, and of medical practice.

We can hope for no improvement through laws which make postmortem examination compulsory; hence it is necessary to determine, if possible, some of the causes underlying the present hostile attitude. If we can know causes, we may be able to overcome them to a greater or less degree by other than legal means, education being the chief one. It must be remembered, however, that not only the laity, but also a part of the medical profession, needs education. Almost every hospital staff has a few members who not only make no effort to obtain consent for postmortem examination of their cases, but who may even actually frown on any exertion to this end put forth by the pathologist, the intern or the administration of the hospital.

Factors other than ignorance and indifference have probably received a larger share of blame than they deserve. Religious objection is frequently mentioned

as an insuperable obstacle to obtaining consent for necropsies, especially in those hospitals a large proportion of whose patients are Catholics or Jews. The essential factors in such hospitals, as in all others, are ignorance and indifference, rather than religious belief. My first experience was in a Catholic hospital whose governing Sister Superior was so broad minded and intelligent that she herself frequently accepted the responsibility of ordering a necropsy, knowing that she could overcome objections based on religion alone; the result was a high percentage of necropsies in a hospital which previously had had very few. At the Mount Sinai Hospital of New York the necropsy percentage has been increased, by well directed effort, from a negligible figure to more than 50 per cent., and at the Michael Reese Hospital of this city the latter figure is also being approached during the present year. Such experiences indicate that religion is not an insurmountable barrier to the development of a worth-while postmortem service. The attitude of the hospital staff and of the hospital administration is a much more important factor than religion or other factors that might be mentioned.

While objection to postmortem examination is a general condition, the percentage of permission necropsies varies in different hospitals, communities and localities, indicating that lack of effort is perhaps as much to blame as lack of knowledge. How unsatisfactory conditions are in Chicago is indicated by the figures published by the Institute of Medicine of Chicago. In 1920, in a total of thirty-nine hospitals, not including Cook County Hospital, whose percentage was 12.7, there were 4,868 deaths, in only 12 per cent. of which permission necropsies were made. In six of the hospitals, the percentage was 20 or over, ranging from 20.1 per cent. to 52.2 per cent. for this group; in seven it was from 10 to 20 per cent.; in ten, from 5 to 10 per cent., and in nine, from 1 to 5 per cent. These figures are not of such a magnitude as to induce an egotistic overdevelopment of local pride; the highest percentage attained by all of the hospitals, 52 per cent., should be the minimal aim. The opposition of the Chicago Asso-

ciation of Undertakers is a local factor of importance. While this organization, through its governing board, has taken a stand that will not permit a hearing of intelligent arguments, many of the members of the association, as individuals, are amenable to reason and can be quite helpful. So far as the local situation is concerned, I am inclined to agree with the statements of the committee of the Institute of Medicine, that "while prejudice and ignorance, together with religious scruples, account for much of the difficulty encountered in obtaining permission for necropsies, the alleged prejudice against necropsies is not so great as has been assumed," and that "indifference in the matter of necropsies often goes hand in hand with professional indifference as to correctness of diagnosis and treatment."

It might be argued that, although there is a paucity of necropsies in this country, surgical material should be ample for the development of pathology. Of such material there is certainly no dearth, and much of it is of value. It is difficult to understand how the surgeon, through whose hands passes a wealth of material in a condition ideal for study, can do otherwise than become a competent pathologist; mere contact with the material, aided by good eyesight, should do the work. As a matter of fact, however, one of the striking features of surgery in this country is the rarity of the surgeon who knows pathology. For most surgeons the chief point of interest in abnormal tissues is the technic of their removal, rather than the condition which the tissues may show or the processes that have been active. The attitude of the surgeon toward the tissues that he removes is only part of our general reaction of indifference to the development of pathology; and until we acquire a deeper interest in general pathology in this country, we cannot hope that the surgeon or other specialist will become adequately trained in this science. While, therefore, surgical material should offer a fruitful field for study, it will not be fully utilized until a change in the lay and professional attitude toward postmortem examination shall have brought about a broader knowledge of pathology on the part of the profession as a whole.

Still another general factor that retards the development of pathology is the absence of an American journal devoted primarily to pathologic anatomy and histology. We have nothing in this country comparable to *Virchows Archiv,* Ziegler's *Beiträge,* or the *Frankfurter Zeitschrift für Pathologie,* journals whose influence on modern pathology, even today, cannot be measured. Because there is no similar publication in this country, the pathologist hesitates to submit a paper on a purely pathologic subject to any of the existing journals. Since he knows that he will have this hesitation in connection with the completed work, he hesitates to begin the work at all. The result is an inadequate presentation of even such material as does become available. There is no doubt that such a journal would be a great stimulus to the publication of valuable work; no other one thing would be so immediately effective.

EXPERIMENTAL RESEARCH

Our existing journals reflect the tremendous development which experimental medicine in all its branches has made in this country. This development, due in part, at least, to the stagnation of pathology caused by lack of material, has, in its turn, led to further retardation of pathology. For many, experimental work on animals, in the absence of human pathologic material, becomes a path of least resistance. The spectacular results occasionally obtained in experimental work have also helped to enhance the importance of such work. The increasing number of full-time clinical teaching positions has directed the energies of a large number of investigators into experimental work of clinical application. As a result of these and other factors, experimental research in the United States has reached a development of which we may well be proud. But without laying oneself open to the charge of belittling experimental research, one may be permitted to express a fear of certain tendencies that are manifesting themselves. Of these, one is the greater emphasis sometimes placed on "experimental" than on "work"; merely because a piece of work is experimental in char-

acter, it may receive a greater measure of credit than the work itself actually deserves. The great desire to do something experimental, because experimental research now occupies the center of the stage, may lead to the carrying on of work whose inception was not preceded by proper conception, by the thought and planning and imagination that every problem should receive before the actual attack on it is begun. And in the interpretation of results there is sometimes apparent a lack of calm contemplation and of knowledge of underlying principles which is characteristic of mediocrity. Imagination and speculation have no place in the reading of the actual results of experimental procedures, but they should have a part, when properly controlled by sound judgment, in the planning of work and in the discussion of its applications. The philosophic type of mind is not being developed to the degree that one might wish. This may be due, in part, to the fact that much of our experimental research is being done by younger investigators, who have not reached the age of contemplation and reflection, and who work more from without than from within. While mental youth, so valuable because of the enthusiasm and energy which it applies to work, may be an element in our present tendencies, one may express the fear that the latter are not such as will lead to the development of philosophers, even under the mellowing effect of advancing years.

Experimental research needs a period of reflection and introspection, in order that it may properly correlate its findings. It needs occasionally to measure its results in terms of pathology in order to be sure that it is not going astray. The development of the experimental sciences, instead of retarding pathology, should lead to a fuller flowering of the latter. Pathology, for its further advancement and interpretation, needs to have applied to it the results which have been obtained by the application of experimental methods to all the other sciences. Virchow and his successors carried us to the border of the cell; it remains for the newer research to admit us into the cell itself. The cellular pathology of Virchow must become the intracellular

pathology of the future. But while we are waiting for the full development of the latter, it is necessary to keep alive an interest in pathology as we already know it; we can build for the future only on the knowledge of the past. Biologists with a wide knowledge of cytology, chemistry or physics will find in pathology, not a dead subject that is to be disregarded, discarded and forgotten, but a most interesting field for study if they will but remember that end-results are not so important as processes in pathology. I would, therefore, plead that our future development be not entirely at the expense of pathology, and that in the evaluation of work done, that of the pathologist be not entirely discredited. Pathology must still continue to be the foundation of clinical medicine; medical practice can be no better than its basic element. And pathology must be the final measure for determining the value of our experimental work and its applicability to the problems of human medicine.

INFLUENCE OF LOCAL SOCIETIES

While some of the factors that hinder the development of pathology are general in character, rather than local, and are not to be overcome by the endeavors of any local group of individuals, it has seemed to me that our local societies can perform a most useful function in maintaining an interest in pathology. This is my reason for making this plea for the development of pathology before this society. It should be our aim to enlist the interest of the clinician as well as of him who is concerned primarily with pathology and its related subjects. The clinician should be stimulated to learn pathology, not merely by listening, but by presenting his own interesting material. The younger workers who are engaged in the laboratory, either permanently as a life work or temporarily previous to going out into practice, should be urged to present the products of their labors from time to time, in order that the results of their experimental and other work may have the widest possible application. For keeping the lamp alight, a local society such as this is the most important agency.

A GUINEA-PIG EPIZOOTIC DUE TO A PARATYPHOID B BACILLUS

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AND
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In the spring of 1920 the death-rate of the guinea-pigs of the stock of the Nelson Morris Institute began to increase. The increase at first was slight and little attention was paid to it. By the middle of summer the death-rate had increased to such an extent as to indicate the presence of an epizootic disease. The infection was not brought under control until the end of the summer, by which time over 500 guinea-pigs had died.

In animals, which died in the earlier part of the epizootic, the pathologic changes were those characteristic of the so-called pseudo-tuberculosis of rodents. The spleen was enlarged and studded with tubercle-like abscesses. The liver contained similar lesions, as well as areas of focal necrosis or larger necroses with little cellular infiltration. The pleura and peritoneum were thickened and adherent in some animals, and in females which had recently given birth to young the uterus was frequently involved.

As the infection assumed epizootic proportions, the animals died without distinctive lesions, but with positive bacteriologic blood and organ cultures. The lesions of hemorrhagic septicemia were absent at all stages.

Pregnant and parturient females were especially susceptible, as were also the young of both sexes. Older males suffered much less severely.

From all the animals examined bacteriologically there was isolated a gram-negative, motile bacillus, which belonged culturally to the paratyphoid-enteritidis group of colon-typhoid intermediates. The organism was isolated from the heart's blood and from such gross lesions as were present. The isolated bacillus was highly virulent for guinea-pigs on sub-

cutaneous, intraperitoneal or intravenous inoculation, and on feeding. White rats, white mice, and rabbits were susceptible to artificial inoculation, but rabbits which were kept in the same building with the guinea-pigs escaped spontaneous infection.

By its cultural reactions the organism was not to be differentiated from a typical human strain of B. paratyphosus B and from B. enteritidis (Table 1). It could be differentiated readily from B. suipestifer. In the tables our organism is designated A 5.

In its agglutination reactions (Table 2), the guinea-pig organism showed relations only to B. paratyphosus B of human origin, and was quite distinct from the other three fixed intermediate species. Two guinea-pig strains, Nos. 240 and 244, and one rabbit strain, No. 245, received from Professor Jordan's laboratory, were closely related to our organism and showed the same immunologic relations to the other intermediates as did our A 5. Agglutinin absorption experiments indicated that our organism was not identical with the Jordan animal strains (Table 3). The strain included in Table 2 as B. paratyphosus B (Army) was an atypical para-B both culturally and immunologically, and has since been identified as a B. aertrycke strain, Newport type, of human origin. Our A 5 showed not the slightest serologic relationship to this organism, although many of the rodent intermediates have recently been found to be closely related to B. aertrycke, especially those strains of mutton origin.

Complement fixation and opsonic experiments yielded less clear-cut results than the agglutination experiments.

Immunization of the guinea-pig stock by a polyvalent killed vaccine made from several strains isolated during the epizootic led to the development of agglutinin titers up to 1 : 160 in the immunized animals. The latter were protected against living organisms in feeding and inoculation experiments. Immunization of the entire stock was followed by disappearance of the infection.

TABLE 1.—CULTURAL REACTIONS

	Lactose	Dextrose	Xylose	Arabinose	Dulcitol	Litmus Milk 24 Hrs.	Litmus Milk 6 Wks.	Lead Acetate 24 Hrs.
B. paratyphosus A (Army)..	0	AG	0	AG	AG	A	A	0
B. paratyphosus A (Jordan)	0	AG	0	AG	AG	A	A	0
B. paratyphosus B (Army)..	0	AG	AGs	AGs	AGs	Alk.s	Alk.	Dark
B. paratyphosus B (Jordan)	0	AG	AG	AG	AG	Alk.	Alk.	Dark
B. suipestifer.....	0	AG	AG	AGs	AGs	Alk.s	Alk.	0
B. enteritidis.....	0	AG	AG	AG	AG	Alk.s	Alk.	Dark
A 5.....	0	AG	AG	AG	AG	Alk.s	Alk.	Dark

A = acid; G = gas; s = slight; Alk. = alkaline.

TABLE 2.—AGGLUTINATION REACTIONS

	Suspensions									
	B. paratyphosus A		B. paratyphosus B							
Serums	(Jordan)	(Army)	(Jordan)	(Army)	B. suipestifer	B. enteritidis	A 5	No. 240	No. 244	No. 245
B. paratyphosus A (Jordan).....	1:10240	1:320	0	1:320	0	0	0	0	0	0
B. paratyphosus A (Army)	.....	1:5120	.....	1:10	0	0	0	0	0	0
B. paratyphosus B (Jordan).....	0	1:20	1:10240	1:1280	0	0	1:160	1:320	1:640	1:2560
B. paratyphosus B (Army)	.....	1:10	.....	1:2560	0	0	0	0	0	0
B. suipestifer	.....	0	.....	0	1:5120	1:1280	0	0	0	0
B. enteritidis	.....	0	.....	0	1:1280	1:5120	0	0	0	0
A 5.....	.....	1:10	.....	0	0	1:20	1:10240	1:5120	1:2560	1:1280
Normal.....	0	0	0	0	0	0	0	0	0	0
None.....	0	0	0	0	0	0	0	0	0	0

TABLE 3.—AGGLUTININ ABSORPTION

	Suspensions			
Serum A 5 Absorbed with	A 5	No. 240	No. 244	No. 245
A 5.....	0	1:30	1:60	1:60
No. 240.....	1:40	0	0	0

November 14, 1921.

COCCIDIOIDAL GRANULOMA; DEMONSTRATION OF SPECIMENS

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The specimens shown here are from a case with the following history:

A man G. L., now 32 years of age, in 1911 went to California from Chicago and worked in the Mojave desert with a surveying crew. His right ankle became chafed and badly infected. After six or eight months he could not use it and was seen by Dr. Norman Bridge at Los Angeles who pronounced it an infection with oidium coccidiodes. At that time his right foot was amputated above the ankle. After this he used an artificial foot and could work, dance, etc. Some three years ago his left ankle became involved in a similar way and later became ankylosed. Also lesions of a similar character appeared on his body which were from time to time lanced to release pus after which they would slowly heal.

Two months ago fresh lesions appeared on either side of his left ankle which increased in size and were curetted down to the bone. The results were not satisfactory and an amputation was made several inches above the ankle joint. The patient still has lesions on other parts of the body. Several Wassermann tests have been negative.

On the amputated foot (Figure 1) are four open lesions the one on the inner side, having been curetted, is large with a ragged base and rather clear cut prominent margins. The skin around them is discolored and the lesions all have margins undermined often to a distance of two or more centimeters by a necrotic gelatinopurulent exudate which in places reached bone, tendon and muscle. Smears, cultures and sections were made from these lesions.

In the smear preparations were many spherical double-contoured bodies varying roughly from five to thirty microns in diameter. No budding forms or

mycelial filaments were seen. Definite intracellular spore like bodies appeared in some of the organisms.

On plain and sugar agar the organism appeared as a white fluffy growth above with definite penetration into the media beneath. In broth the growth was a flocculent one. The growth on artificial media was made up of branching septate mycelium with numerous aerial hyphae carrying elongated or rectangular spores.

Microscopic sections of the tissues revealed a chronic granulation tissue made up of lesions quite like tubercles. Within many of the giant cells which were common were round or oval organisms usually near one end of the cell. Caseation was not marked.

Subcutaneous injection of the organism into guinea-pigs caused after ten days to two weeks a large localized abscess the size of a walnut with abundant purulent and partly caseous content together with involvement of regional tissues and distant organs. Smear preparations revealed very large numbers (often twenty-five to the oil immersion field) of the characteristic double contoured bodies, some of which contained numerous intracellular spore-like bodies. No budding or mycelial forms were noted. The organism was readily recovered from the pigs on artificial media. Death occurred later with miliary involvement of lungs, spleen, liver, pleura and peritoneum.

The organism conforms to that first described by Wernecke [1] in South America and later by Rixford and Gilchrist [2] in similar cases and named by them coccidiodes immitis. Some thirty or more cases have now been reported nearly all of which have appeared in California in or near the San Joaquin Valley.

Studies of this disease have also been made by Ophüls,[3] Hektoen,[4] Brown,[5] MacNeal and Taylor,[6] Evans,[7] and others.

Pusey [8] described a case from the Cook County Hospital in a Polish woman who had not been out of the

1. Cent. of Bact., 1892, 12, p. 861.
2. Johns Hop. Hosp. Rep., 1896, T. 209.
3. Jour. Exper. Med., 1902, Vol. 6, 443.
4. J. A. M. A., 1907, 49, p. 1071.
5. J. A. M. A., 1907, 48, p. 743.
6. Jour. Med. Res., 1914, 31, p. 261.
7. J. Infect. Dis., 1909, 6, p. 523.
8. The Principles and Practice of Dermatology, W. A. Pusey, 3rd edition, Appleton & Co., p. 812.

city for years. No other cases are known to have appeared here in Chicago.

Oct. 9, 1922.

CARCINOMA OF THE SMALL INTESTINE

SIDNEY A. PORTIS

Carcinoma of the small bowel is a comparatively rare lesion. Ewing states that it comprises 3 per cent. of intestinal carcinoma. Of the 41,858 necropsies at the Vienna General Hospital, 3,585 were cases of carcinoma. Of these 343 were in the bowel and only eleven of these were in the small bowel. Hinz found among 584 cases of carcinoma of the intestinal tract, that only eighteen were located in the small bowel. Johnson, in a recent paper, reported two cases of carcinoma in the jejunum and one in the ileum. Bevan reported five cases of cancer of the jejunum. Cancer of the duodenum is reported by Lichty in six cases, McGuire four cases, Herman two cases, Jefferson, Deaver and Head each one case. Judd reported twenty-four cases, five of which were in the duodenum, eleven in the jejunum and six in the ileum, and two multiple cases. About 70 per cent. of the cancers of the duodenum are located at the ampulla.

These tumors of the small intestine, according to Ewing, are of three distinct forms:

1. Part of a local or general intestinal polyposis. This is rather rare in the small intestine, being more frequent in the colon. This type probably explains the occurrence of multiple carcinoma with several strictures produced.

2. Multiple or single benign embryonal carcinoid tumors, which are usually found in the ileum and jejunum in the form of single or multiple firm opaque nodules as large as a pea or bean. They lie in the mucosa or submucosa. In stricture they form three groups:

(*a*) Pancreatic island tissue;
(*b*) Heterotropic intestinal mucosa;
(*c*) Brunner's glands.

3. Localized adeno-carcinoma arise under various conditions—from single intestinal polyps, and tend to maintain an adeno-carcinomatous structure. The majority of the intestinal carcinomas are of this type. When ulceration is delayed, the tumors may reach sufficient size to obstruct the lumen. Ulceration and stricture more commonly result. Metastases are present in about one third of the cases, and involve the mesentary, liver, lungs and peritoneum.

The clinical picture is variable, depending on the type and age of the carcinoma. In the early cases, before obstruction, there may be no subjective symptoms, and the patient may not be aware of the presence of the tumor until obstructive symptoms appear. Although hemorrhage is uncommon, yet even in the earliest stage erosion occurs, and occult blood is found in the stools. This is of greatest importance in an early diagnosis.

As is common in carcinoma in any part of the body, a loss of weight and an anemia take place. Asthenia and a vague abdominal discomfort are complained of. Later pain is felt, and this increases as obstruction begins. It may be colicky and paroxysmal, especially when there is much tympanites. A progressively developing constipation is complained of, especially with definite stenosis at the tumor site. At times constipation does not appear at all, but diarrhoea is present. Rarely constipation alternates with diarrhoea. Very soon stomach symptoms appear. Belching and nausea, anorexia and thirst are complained of, and later vomiting begins. The vomiting is frequently repeated as often as six to eight times daily, and the vomitus is usually of a greenish color. In a well developed case it may have a brownish color and a fecal odor. The typical picture of intestinal obstruction appears with the closure of the stricture.

The triad of symptoms which are of diagnostic value is a stubborn constipation, with or without alternating diarrhoea, severe attacks of colicky pain, and vomiting.

Objective symptoms are not found early, but with developing stenosis there is tympanites, visible peri-

stalsis, and a tumor may be palpated. The tumor is usually small and firm. It is movable and changeable in location. With marked vomiting there may be pronounced dehydration and signs of severe intoxication.

Laboratory studies of the gastric contents do not show evidence of disease. The stools rarely show gross blood, but occult blood is usually found, and is the most reliable of the early findings. The roentgen ray is of great help in the diagnosis. A normal stomach and duodenal bulb help to rule them out as a cause for the occult blood. The duodenum is usually dilated, and, likewise, the small bowel proximal to the stenosing tumor. Gas and fluid are found in the distended bowel. The amount of dilatation found will naturally vary with the duration of the tumor, and the amount of stenosis produced by it. In the cases in the literature, an early diagnosis was not made, and only at operation for acute obstruction was the tumor found. This is too late for a cure. A routine examination of all stools for occult blood will be of decided help in discovering these lesions early enough for operative aid. In the differential diagnosis, tuberculosis must be ruled out carefully. Actinomycosis at times gives a similar picture and rarely syphilis.

REPORT OF CASE

Male, 34 years old, complained of epigastric distress, vomiting, loss of weight, weakness, night sweats and tinnitus. For the past six weeks he had had abdominal distress with swelling on the left side. The swelling was intermittent and accompanied by cramp-like pains, and visible peristalsis. Vomiting occurred at a later stage, and he brought up food eaten twenty-four hours or more. At times the vomitus had a fecal odor, and was green to yellow in color. The trouble came on at intervals. At first the attacks occurred once a week, but later as often as twice a week. Between attacks he felt fairly well. An enema brought no relief. In the past six weeks he lost 20 pounds, and felt very weak. He had had no night sweats. Constipation began several weeks before and was now very stubborn. Bowels would not move without an enema.

Physical signs of the heart and lungs were normal. The abdomen was distended, but no peristalsis was visible. No mass could be felt. There was tenderness on the left side,

just above the level of the umbilicus. The stomach test was normal, except for delay in emptying. The stool showed a marked reaction for occult blood. His Wassermann test was negative, and there was a secondary anemia. The Von Pirquet test was slightly positive. The urine showed a high indicanuria.

The roentgen ray showed normal chest findings. The stomach was in a transverse position, but was normal in its findings. The duodenum was dilated. The small bowel near the duodenum was filled and remained so, giving the appearance of a stomach with air space above a fluid level. The bowel at the point distal to the dilatation showed a definite constriction. Reversed peristalsis was seen in the dilated portion proximal to the constriction. Operation was advised for a probable tumor of the jejunum. Dr. Christofferson found an annular growth in the jejunum near the ileum. A resection and a lateral anastomosis were carried out.

A specimen of the excised tumor was shown to Dr. Schultz, who reported as follows:

"Gross: Resected segment of small intestine 5 cm. long. At its middle there is a rather sharp constriction 2 cm. in external diameter, in which the external surface for half the circumference is formed by a slightly raised, firm, pale area 1 cm. wide in the longitudinal axis of the gut. Above the constriction the gut is 4 cm. in diameter, below it, 2.5 cm. In the region of the constriction a pale, rather dense, well defined, mushroom mass projects into the lumen. This is 2 cm. wide in the long axis of the gut.

Microscopic: Both above and below, the transition of normal mucosa to tumor is sudden and sharp. The tumor is composed of stroma of variable density, in which are embedded atypical glandular alveoli. The latter vary in shape and in size; many are branched, and in many the epithelium is infolded. The epithelium in general is of the intestinal cylindrical type, but in many alveoli it is more atypical and polyhedral. Mitoses are numerous. The entire intestinal wall is penetrated by the tumor mass, which has replaced muscle and the other constituents of the wall."

Oct. 9, 1922.

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PRIMARY CARCINOMA OF THE LUNG

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Primary carcinoma of the lung, while a comparatively rare affliction, is not of sufficient rarity to be considered a curiosity. Because of its complicated clinical picture and because it is so frequently incorrectly diagnosed, it should be kept in mind.

Incidence.—Various authors have stated different percentages for the frequency of carcinoma of the lung. Moise considers this neoplasm to occur in about 1 per cent. of all malignancies and about 0.3 per cent. of all necropsies. Reinhard at the Dresden City Hospital found five cases in 545 cancers. Fuchs found eight cases in 12,307 necropsies in Munich. Ewing places the incidence at 1 per cent. Kaufmann quotes the statistics in Basle as 1.76 per cent. and in Breslau as 1.8 per cent. Scott & Forman had three examples in 302 cases of carcinoma. Wiczkowski collected 126 cases in 11,093 autopsies. Weller concluded that it occurred in 0.3 per cent. of all autopsies.

We have had one case, the present one, in the last 362 autopsies at Michael Reese Hospital, A. V. St. George collected only six cases of carcinoma in the Bellevue Hospital over a period of eleven years. Barron places the frequency as 2 per cent. of all cancers.

From the above reports it is seen that primary carcinoma of the lung occurs in about 1 per cent. of all malignancies and in about 0.3 per cent. of all necropsies.

Etiology.—Males are much more frequently afflicted than females. The average frequency is about 85 per cent. in the male sex.

Age.—The majority of cases occur between 40 and 70 years, with the greatest frequency between 60 and 70. Kaufmann reports a case at the age of 30. Hall and Tribe report a case occurring at the age of 17. Haynes and Gaskell had a case at the age of 27.

Previous Diseases.—Ewing, in a very elaborate discussion, considers a preexisting pulmonary disease as a very definite predisposing factor. Among these he lists pulmonary tuberculosis, pulmonary infections of various types, bronchiectasis and bronchitis. Scott and Forman believe its predominant occurrence in males is due to heavy smoking and the inhalation of chemical vapors of the industrial world. Adler found that traumatism was present in 4 per cent. of his collected cases. Margaret Uhlig in discussing the Schneeberger Krebs, the endemic carcinoma occurring in Saxony among workers in cobalt mines, considers the injury to the bronchial mucosa from inhalation of dust and metallic particles a definite predisposing factor. Haythorn found in autopsies on miners dying from pneumonia that there frequently existed various degrees of metaplasia of the bronchial mucosa.

The right lung is involved twice as frequently as the left. Weller believed that this was due to the larger size of the right bronchus and that it is more accessible to irritation and more frequently the seat of pulmonary disease.

Ewing believes that a certain number of primary carcinomas of the lung originate from the overgrowth of misplaced fetal portions of the bronchial tree, overgrowth of fetal bronchiectasis, from bronchial malformations, from embryonic displacement of islands of squamous epithelial cells or from a preexisting tumor usually a bronchial papilloma.

Type of Growth.—The seat of origin of primary carcinoma of the lung is generally conceded to be either from bronchial mucosa, bronchial mucous glands or from pulmonary alveoli. Ewing considers the frequency of bronchial mucosa carcinomas as being 32 per cent.; Weller 25 per cent., and Wolff 50 per cent.

The gross appearance of primary carcinoma of the lung is quite varied. It may be a diffuse or a nodular tumor (Ewing); or it may be a circumscribed growth (Kaufmann). The tumor usually is of a white or yellow color, but may be hemorrhagic, especially when associated with either preexisting or coexisting cavities

which have undergone ulceration. It may be rather firm or scirrhus in nature or softer and medullary. The growth may be very extensive and cause a complete consolidation of the lung resembling a pneumonic involvement (Ribbert). The cut surface may reveal an extensive bronchiectasis with purulent bronchitis. Plugs of tumor tssue may fill the bronchi and smaller bronchioles. Frequently there is peri-bronchial growth which causes stenosis of the bronchi (Aschoff). LeCount and Davis reported a case in which the mucosa of the trachea and larger bronchi resembled skin.

Method of Propagation.—Like all the malignancies, this type of tumor may spread along the peri-bronchial or peri-vascular lymphatics, but there is a peculiarity of certain types of primary carcinoma of the lung, as described by Ewing, in which the growth starts at the bifurcation of the trachea or larger bronchus, and grows upward and downward, filling up the smaller bronchi and bronchioles with tumor tissue. Kaufmann emphasizes the frequency of retrograde dissemination along the lymphatics, which may eventually involve the pleura and cause pleural effusion. Various complications may arise. As the result, either of stenosis of the bronchi by peri-bronchial involvement of the tumor or of intra-bronchial growth of the tumor, bronchiectasis frequently develops and becomes associated with purulent bronchitis. Cavities may form (Kaufmann) due to a disintegration of the tumor tissue, possibly as the result of lack of nourishment. These cavities may contain very putrid debris and frequently resemble tuberculous cavities. Hemorrhage may occur (Moise) although rarely of any marked degree.

Histology.—The tumors arising from the bronchial mucosa are usually either of the squamous epithelial type and result from metaplasia of the bronchial mucosa or they may be composed of cylindrical cells which have not undergone metaplasia, the resulting tumor being glandular in character (Ewing). The histological appearance of the squamous cell carcinomas resembles that of the usual type of this growth, form-

ing solid alveoli with epithelial pearls, inter-cellular bridges and in some instances keratin. It is very interesting in many cases to see the definite metaplasia of the columnar bronchial mucosa to squamous epithelium and this metaplastic tissue giving rise to the squamous cell carcinoma, a condition beautifully illustrated by the case which I am reporting. The tumors originating from the bronchial mucous glands are usually composed of short cylindrical or cuboidal cells forming cord-like alveoli, some containing a cavity and frequently producing a large quantity of mucus. The bronchial mucosa is usually intact and it is this type of growth that frequently causes bronchial stenosis (Kaufmann). The tumors arising from the pulmonary alveoli are usually composed of cylindrical or cuboidal epithelium, which form many infoldings and papillary projections into the lumina; this form is recognized by the extensive involvement of the pulmonary parenchyma with relatively slight involvement of the bronchial lining epithelium in the absence of demonstrable connection with the bronchial mucous glands (Moise). This type may be a very diffuse nodular growth and may cause a uniform consolidation (Ewing).

Metastases.—There are few organs in the body which fail to appear as possible sites for secondary involvement (Ewing). A rather frequent site for metastastic growth is the brain; when cerebral metastases occur they usually predominate the clinical picture (Aschoff). Scott and Leist have found that 14 per cent. of the cases show bone metastases. Moise, discussing the frequency in which the various organs are involved lists them as follows: regional lymph nodes, the liver, kidney, other portions of the lung, brain, pericardium, etc.

Clinical Picture.—The clinical picture is usually dominated by the pulmonary findings, although there are certain cases in which the metastastic growths, especially those that are in the brain, may predominate the picture. However, the pulmonary findings usually are cough, dyspnea, hemoptysis, pain, recurring pleural effusion, pressure symptoms referable to the mediastinal

structures, tumor fragments in the sputum, loss of weight, and the roentgen ray findings of the tumor growth in the place of normal lung parenchyma. Death is usually due to asphyxia, hemorrhage, pulmonary edema with secondary pneumonia, thrombosis or generalized metastases.

PRESENTATION OF CASE

Male, aged 43.

Clinical Diagnosis.—Pleurisy with effusion in right chest; compression of the right upper lobe; emphysema of the left lung.

Anatomical Diagnosis.—Primary bronchial carcinoma originating in the right main bronchus, causing complete obliteration of it and the remainder of the bronchial tree supplying the right lower lobe. Bronchiectasis with purulent bronchitis of the lower lobe of the right lung. Purulent bronchitis of the right upper and middle lobes. Carcinomatous metastases in the visceral pleural over the right lung. Bilateral fibrous adhesive pleuritis of both lungs. Marked dilatation of the right ventricle. Fibrous peri-hepatitis, peri-splenitis and peri-cholecystitis.

Clinical History.—The patient had been previously in the Winfield Sanatorium. He entered Winfield on September 30, 1921, because of weakness, loss of weight, and cough. Physical findings at that time revealed some apical findings and impaired resonance over the right lower lobe. The diagnosis at that time was of moderately advanced tuberculosis. However, sputum examination on seven occasions was consistently negative. The blood showed 5,630,000 red cells; 11,200 white cells and Hb 80. He ran very little temperature previous to April 14, 1922, but after that period the temperature ranged from 97 to 104 degrees at varying times. On April 14, 1922, the patient was supposed to have developed a pleurisy with effusion, but aspiration of the chest did not reveal any fluid. The roentgen ray at that time showed consolidation in the right lower lobe with the appearance of fluid. The trachea was somewhat flattened and it and the bronchial tree were drawn to the right.

The patient entered Michael Reese Hospital on May 6, 1922, with the symptoms as given above. The physical findings at that time revealed:

Chest: Flatness over the entire right chest with increased fremitus over the upper and middle lobes but decreased over the lower lobe of the right lung. The left lung was apparently normal except for some increased breath sounds over the apex.

Heart: Heart was pushed over to the right, otherwise nothing abnormal was found. The blood pressure was 116 systolic and 78 diastolic. On May 8, 1922, the chest was aspirated but no fluid was obtained.

He remained in much the same general condition and on June 4 developed a definite stridor with retraction of the upper part of the chest. On June 5, Dr. Sonnenschein examined the patient and found the laryngeal mucosa very pale, the trachea was twisted and pulled toward the right so that it was impossible to see the bifurcation. The patient was up and about and in fair condition until 10 p. m., July 1, 1922, when he suddenly developed a very severe attack of dyspnea, cyanosis and an imperceptible pulse. Considerable stimulation was given but the patient died at 12 p. m.

Laboratory findings: The sputum did not reveal any tubercle bacilli. The urine at times showed a few casts and a trace of albumin. The blood count showed a leukocytosis ranging from 12,400 to 23,100.

Roentgen ray: Roentgen ray revealed a dense shadow in the right thorax; the trachea being pulled over to the right and the pericardial cavity also pulled over to the right. The process appeared to be one of fibrosis whereby the heart and mediastinum were pulled over into the right chest. It was impossible to determine whether or not this was caused by fluid or thickened pleura.

On June 6, 1922, a second examination was made and showed the lung to be clearing up to a moderate degree. The temperature during his last illness showed only a degree or more elevation.

Necropsy.—The body is that of a well nourished and moderately developed white male of about 40 years of age, measuring 162 cm. in length. The superficial lymph glands are not palpable. There is no icterus present and no edema of the extremities. The external genitalia reveal no abnormalities.

Abdominal cavity: The peritoneal cavity does not contain an excess of fluid. The peritoneal surfaces are smooth and shiny. The gall bladder is densely bound down by fibrous adhesions to the liver and duodenum. The spleen and liver are bound down posteriorly by fibrous adhesions. The appendix is free and unchanged.

Thorax: The right pleural cavity is completely obliterated by dense fibrous adhesions over the lower two lobes. It contains about 250 c.c. of fluid in small pocket-like formations. The left pleural cavity is obliterated posteriorly and laterally over the lower lobe.

Pericardial cavity: The pericardial cavity does not contain an excess of fluid and its surfaces are smooth and shiny.

Lungs: The right lung reveals a complete consolidation of the lower lobe, with moderate consolidation of the middle and upper lobe. The pleural surface over this lung reveals many small shot-like nodules measuring about 3 to 5 mm. in diameter. There are also some fine cord-like streaks on its surface. The cut surface reveals in the lower lobe an extensive bronchiectasis, the cavities ranging from 5 mm. to several centimeters in diameter and each filled with a very thick purulent exudate. The bronchi proximal to these cavities are filled with a dense yellowish white tissue. The cut surface of the upper two lobes reveals some lesser degree of bronchiectasis and considerable purulent exudate can be expressed from them. The main bronchus supplying the right lung is partly filled by a tumor mass measuring 5 by 4 by 2 cm. and which extends into the beginning of the trachea for about 4 cm. This mass is not adherent to the trachea, but seems to have originated from a dense adherent mass which completely obliterates the lower bronchus supplying the right lower lobe. These tumor masses seem to have originated from this bifurcation of the right bronchus and have been propagated along the entire bronchial tree of the right lower lobe. There is very little tumor tissue in the bronchi supplying the middle lobe and practically none in the bronchus supplying the upper lobe. The cut surface of the left lung reveals nothing abnormal except a slight edema.

Heart: The right ventricle is in marked diastole. The aorta and pulmonary artery reveal no changes. The wall of the right ventricle measures 3 mm. The left ventricle measures 15 mm. and is in firm systole. The myocardium reveals no gross abnormalities.

Gastro-intestinal tract reveals nothing abnormal and no tumor masses can be found in it.

Liver: Liver is somewhat enlarged. The lobules show some central congestion, but otherwise nothing abnormal.

Spleen: The spleen is slightly enlarged and its pulp congested.

Gallbladder: The gallbladder and gall tracts show no changes, except for the dense adhesions mentioned above.

Genito-urinary tract: The kidneys are of normal size. The capsule strips easily leaving a smooth surface. The cut surface does not reveal anything abnormal. The adrenals are normal. No tumor masses can be found in any of the sexual organs.

Microscopic Examination.—Heart: The myocardium reveals a slight hypertrophy of the fibers. No fibrosis. The pericardium is rich in fat; coronary vessels are not sclerotic.

Lungs: The lower lobe of the right lung shows a marked atelectasis and increased fibrous tissue. The obliterated alveoli that remain are lined with a low cuboidal epithelium. The bronchi are distended with a purulent exudate and many

Fig. 1.—Section of a large bronchus filled with a squamous cell carcinoma. To the left there is an abrupt transformation of the metaplastic squamous epithelium to the squamous cell carcinoma. Below this metaplasia a bronchus is lined by a normal ciliated columnar epithelium.

of them contain plugs of tumor tissue, some of which completely fill the small and larger bronchi and bronchioles. Several bronchi reveal changes which are characteristic of the type of origin and invasion of the tumor. These changes are characterized by the presence of the squamous cell carcinoma originating from the epithelium of the bronchus and invading in some places the lumen and in other places the

underlying atelectatic fibrosed lung. In numerous bronchi there is a sharp transition between the normal ciliated columnar epithelial lining of the bronchi to squamous epithelium. The metaplastic tissue is the site of origin of the cancerous tissue transformation. The tumor tissue itself reveals the usual characteristics of a squamous cell carcinoma, in which the cells are of the definite squamous cell type with pearl formation, production of keratin and the formation of numer-

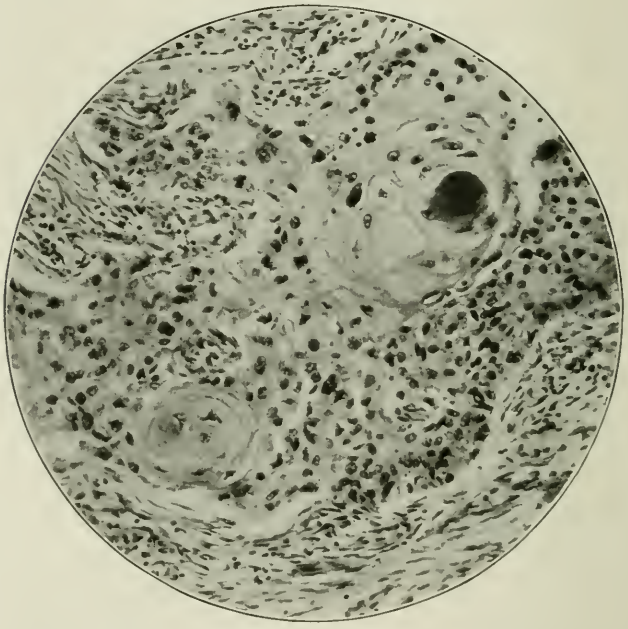

Fig. 2.—Higher magnification of the tumor tissue. There are two distinct epithelial pearls present in the midst of the squamous cell carcinoma.

ous intercellular bridges. In addition, there is a marked variation in the size of the nuclei and of their chromatin content; also there are present numerous atypical mitotic configurations in these nuclei. The upper and middle lobes of the right lung reveal a partial atelectasis and moderated fibrosis of the parenchyma of these lobes. The bronchi are distended with a fibrino purulent exudate. The hilus lymph nodes do not contain any tumor tissue and there is a mod-

erate degree of anthracosis. The left lung does not contain any tumor tissue. The bronchioles are more numerous than is usually the case and they are somewhat dilated. Many of the bronchioles contain a serous exudate and desquamated epithelium and endothelial cells. There is no evidence in any of the bronchioles examined in this lung of the metaplastic process found in the right lung. There is also an emphysematous condition present in the parenchyma of the lung with some fibrosis of the alveolar walls.

Liver: The liver reveals a moderate degree of central congestion. The cells of the liver trabeculae reveal no definite changes except some variation of their nuclear chromatin content. The bile canaliculi contain considerable bile pigment.

Spleen: The spleen reveals some increase of hyalinized fibrous connective tissue. The sinusoids are somewhat more distinct and tend to form definite channels.

Kidneys: There is some protein precipitation in the lumen of the collecting tubules and Bowman's space. The glomeruli do not reveal any abnormalities. In a few areas of the interstitial tissue, there is some increase of connective tissue and round cell infiltration. These are, however, very much limited in extent. The remainder of the secreting and collecting tubules are unchanged.

DISCUSSION

This case of primary carcinoma of the lung introduces several interesting features in the pathogenesis of primary cancer of the lung and the method of its growth.

A very important point to consider is whether or not the bronchiectasis was a primary condition or was a complication resulting from the plugging up of the bronchi and bronchioles with tumor tissue. There was a long standing bronchitis and sufficient pulmonary pathology to have suggested to the clinician that this pulmonary process was one of tuberculosis. There is, however, no bacteriological or pathological finding to substantiate this conclusion.

The atelectasis and bronchiectasis which were seen on gross examination and corroborated by the histological study of the various sections may be the result of a congenital atelectasis or as Ewing has described "an overgrowth of fetal bronchiectasis."

After careful examination of this case, one tends to conclude that the probable origin of the bronchiectasis was due to an overgrowth of fetal bronchiectatic and atelectatic pulmonary tissue. It would appear that if this process were essentially one of fetal origin, a metaplastic transformation would be more probable. An argument against an inflammatory etiology for the extensive metaplasia is that the process was not bilateral.

The metaplastic process seen is undoubtedly a very active one and was still in progress when the patient died. It is extremely interesting that the metaplasia involved numerous bronchi and in most every site there was a transformation of this metaplastic squamous epithelium to a squamous cell carcinoma frequently exhibiting many of the characteristics of this type of epithelial growth, even so far as to produce inter-cellular bridges.

Nov. 13, 1922.

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PRIMARY SPONTANEOUS TUMORS IN THE KIDNEY AND ADRENAL IN MICE*

MAUD SLYE, HARRIET F. HOLMES
AND
H. GIDEON WELLS

Primary tumors of the kidney occur not infrequently throughout the animal kingdom, and, in general, seem to exhibit the same variations and peculiarities seen in human renal tumors. We have reviewed the literature on the occurrence of renal tumors in animals. All told we can find records of but six cases hitherto reported in mice, all being of epithelial character. In rats, both wild and tame, renal tumors are somewhat more frequent; of 156 reported cases of rat tumors twenty-seven were in the kidney, all epithelial despite the fact that the tumors of rats are often sarcomatous. Swine seem to be the only domestic animals in which renal tumors are common, the Wilms type of mixed tumor being most often seen. Renal tumors are not rare in horses, but they are very infrequent in cattle or sheep. No reports of adrenal tumors in mice have been found.

In a series of 33,000 autopsies on mice of the Slye stock, dying natural deaths at all ages, but, as far as possible living out their natural span of life, there have been observed the following cases of true primary neoplasm arising from renal or adrenal tissues: (1) from the kidney, 16 tumors, classified as follows: 1 carcinoma, 3 adenomas, 1 hypernephroma, 7 sarcomas, 3 mesotheliomas and 1 sarcoma of the renal pelvis; (2) from the adrenal, 4 tumors, as follows: 1 cortical adenoma from a misplaced inter-renal adrenal rest, 3 mesothelial tumors; (3) five cases of tumors of the mesothelial structure characteristic of urogenital anlage neoplasms, but the exact origin of which could not be determined because of their widespread growth at the time of death. As these twenty-five tumors occurred

* The complete article is published in the Journal of Cancer Research 6: 305, 1921.

in 33,000 mice presenting not far from 5,000 other tumors, they are evidently uncommon tumors of mice, at least in this particular stock.

It will be noted that in this series there has been no instance of a mixed renal tumor of Wilms type, which is so common a type of renal tumor in man and apparently also in swine. Although inflammatory conditions are very prevalent in the kidneys of mice, epithelial tumors are rare, and especially to be noted is the absence of even a single case of typical malignant hypernephroma, although one benign growth of this type was found. Also, no epithelial tumors of the renal pelvis were found, although there was one case of sarcoma that seemed to take its origin in the pelvis.

Several instances of malignant retroperitoneal tumors have been observed, mostly of sarcomatous structure, which usually invade the kidney. These have not been included in this series, except two cases in which the structure resembled that of the mesotheliomas, suggesting that the tumor had its origin in misplaced rests of the urogenital anlage.

Secondary tumors have never been found in the adrenals, and but rarely in the kidneys. Although this series includes at least 3,000 cases of mammary gland carcinoma, often with widespread metastases in the lungs, we have never seen a secondary growth in the kidney. The only secondary carcinomas of the kidney as yet observed are four cases in which the primary carcinoma was in the lung, thus establishing the true neoplastic nature of these lung growths. In but two cases have metastatic sarcoma growths been seen in the kidney, if we exclude the numerous cases of invasion of the kidney by direct extension from pararenal growths.

As to sex, taking the entire group of renal and adrenal tumors, we have eleven in males and eleven in females, agreeing with the observation made with other tumors in mice that, in tumors not peculiar to the sex glands, there is usually little difference in the incidence in the two sexes.

Differing from the tumors previously studied, coincidence of other tumors with the renal and adrenal tumors is uncommon. One mouse had a spindle cell

sarcoma of the thigh. One mouse in this series had a small, benign papillary adenoma of the lung. Only two mice had a mammary gland carcinoma; of these (21,663) was a remarkable case, for this animal, although but 1 month and 18 days old, had two independent mammary gland carcinomas, osteosarcomas in the spinal column and in a rib, and a mesotheliomatous type of growth involving both kidneys. Except for this unique case there have been practically no instances of malignant tumors in mice less than 4 months of age, and few under 6 months. Most of the renal sarcomas occurred between the ages of 7 months and 1 year, which is somewhat earlier than the usual time of appearance of epithelial growths, which, of course corresponds to experience with human neoplasms.

The epithelial renal-adrenal tumors furnished no illustration of metastasis, but in three cases of sarcomatous or mesotheliomatous growths there was noted involvement of the adjacent lymph glands, in two there were pulmonary, in two hepatic, and in one splenic metastasis, and in one case there were numerous peritoneal growths. The mesothelial type of growths produced the most extensive metastasis and the most widespread infiltration of the body wall.

Oct. 9, 1922.

BISMUTH PASTE TUMORS*

FRANCIS L. LEDERER

From the clinic of Drs. Joseph C. Beck, Harry L. Pollock and Francis L. Lederer, Chicago

Since bismuth paste had been used so extensively in this clinic for so many years in the treatment and diagnosis of suppurating conditions about the head and body, and having within a short period of time observed a series of four cases which presented themselves with obscure findings, following its use, it was deemed advisable to study more carefully the probable course and character of the pathology of such a tumor

* This subject appears in the April, 1923, number of the Jour. of Surg., Gyn. & Obst. in detailed form, together with the photomicrographs, skiagraphs and clinical pictures.

formation. This was done especially, in view of the fact that there is an ever increasing use of bismuth paste and various other modifications and preparations of like nature, with well founded indications, both diagnostically and therapeutically.

Because of the close similarity between tumors caused by paraffin, camphorated oil, vaseline, gray oil, and the tumors brought about by bismuth paste injections, our studies were done along these lines, inasmuch as our preparations contain vaseline and white wax in small amounts. The literature is filled with reports on formation of tumors by the introduction of the above mentioned material and the works of Gersuny, Corning, Moskiewitz, Eckstein, Balzer, Hertel and Leber stand out as foremost in the pioneer work with the injection of these various substances. The majority of these men agreed and some demonstrated conclusively that vaseline is not absorbed in the tissues, whether injected in liquid or solid form, but persists in the state of foreign droplets, and particularly so when protected from muscular contraction and pressure from without.

It is commonly agreed that the introduction of such foreign substances as paraffin, vaseline, camphorated oil and gray oil may produce a traumatic inflammatory reaction which is brought about by tearing, stretching or forcing apart various tissue fibers, leading eventually to the formation of connecting tissue, resulting as in the case of any foreign body, in an attempted encapsulation of the injected material, assuming, of course, that we are dealing with a sterile agent. The small globuli are broken off from the material by muscle contraction, travel and stimulate connective and cell proliferation of the adjoining tissue in their paths. They thus finally get grown together like a sponge and are formed into a meshwork. Hertel, in the work of replacing orbital defects, did excellent work in many series of cases and his deductions are quite interesting. He believes that differing results lie with the differing distribution of the paraffin with regard to the tissue and refers to the work of Leber, who proved that the irritative effects of foreign bodies upon tissues are

augmented if they are finely divided, and that the larger the surface they come in contact with, the more intensive the irritative effects.

However, it is a mooted question as to what ultimately happens to the bismuth vaseline preparation. Dr. J. C. Beck introduced the paste into various sinuses, such as the frontals, sphenoids and antrum, and studied radiographically the length of time the bismuth remains in these cavities, but came to no definite conclusions. Dr. E. G. Beck contends that most of it is found in the dressings within twenty-four hours after injection; in other sinuses, which are deep and tortuous, the paste will remain in them for days and even weeks, and says that frequently it will heal in and become encapsulated and gradually be absorbed through the process of organization of the mass by connective tissue. The latter author also checked up the reaction of living tissues to bismuth paste and this same process was found to go on. His miscroscopical studies showed the border of the bismuth crystals infiltrated with round cells and the spaces between the crystals packed with young connective tissue cells. The border between the bismuth mass and the muscle tissue removed, consisted of several strata of elongated connective tissue cells forming concentric layers and in some places, merging into fibrous bands encircling the bismuth plug. There were also seen a large number of irregularly arranged shorter and longer, spindleshaped cells, which in places invaded the interstices of the adjacent muscular tissue. Whatever the histological findings might have been, Beck thought that radiographic evidence was proof enough that bismuth was absorbed and gave as example lung abscess cavities which were shown in various stages as time progressed and the lung expanded with a diminution of their radioactive contents. Just what happens to this material is not the object of this paper because the experience of Beck and others have long ago considered this phase of the subject in connection with bismuth poisoning and found then that bismuth when absorbed may be found in the cells of the liver, spleen, muscles and intestines.

REPORT OF CASES

Case 1.—Male, aged 25. In November, 1921, had a mild influenza which became complicated by a pansinusitis and accompanied by meningeal symptoms. Went along for two weeks with marked toxic symptoms, when at this time a fluctuating mass was found to be necrotic in an area about the size of a dollar. He was referred to us on Dec. 8, 1921, still complaining of frontal pain. The roentgen ray at this time revealed a bone necrosis in the frontal region with the posterior table apparently intact. Operation was advised and under synergistic anesthesia a radical frontal sinus exploration was done. The mucus membrane lining of the sinus had undergone polypoid degeneration and polype were found blocking the nose frontal ducts. Drainage was established into the nose and the wound closed by interrupted sutures. He was redressed daily; temperature remained normal. On Dec. 31, 1921, bismuth paste (10 per cent.) was injected into both frontal sinuses and the patient was allowed to go to his home. On May 28 the patient returned, having had an uninterrupted course, except for a swelling over the frontal sinus which did not bother him and was not tender. The nasal examination was negative; externally was seen a small tumor-like mass about the size of a half dollar. No fluctuation nor tenderness was elicited and the tumor was hard and not very well defined, being infiltrated into the skin and adjacent tissue. Roentgen-ray examination revealed a bismuth mass in the frontal sinus.

Case 2.—Male, aged 15, Italian. About two weeks before, while at work the patient noticed his neck was getting stiff. He went to his family physician who tried palliative measures, but swelling and fluctuation became so severe that he incised the left side of the neck in two places above the sterno-cleido mastoid muscle. About this time the patient was referred to us in a very toxic state. The areas in the neck were still draining and the patient's condition was very poor. Palliative and general tone methods were carried out. About two weeks later after the acute symptoms had subsided bismuth paste (10 per cent. mixture) was injected into the draining sinuses. It was noticed this time that these sinuses communicated with an area suprasternally but this was thought only to be a communicating sinus. He was injected with bismuth on two successive days and then began to get a series of roentgen-ray treatments to the side of his neck. The patient was discharged with sinuses healed three weeks from the time he was referred to us. About one month later the patient returned with an enlargement in the midline of his neck just above the sternum. It was hard, very slightly tender and seemed to be infiltrating the skin and

adjacent tissues for quite an area around it. It was not well defined. Roentgen ray revealed the masses be made up of bismuth. The patient was advised to do nothing. Then on July 19, under synergistic anesthesia, the tumor was excised. The mass was found to be adherent to the skin and to the substance of the sterno-hyoid and sternothyroid muscles. When removed it measured 2 inches in its greatest width and 3½ inches in length. It had a very hard almost cartilaginous feel and cut with resistance of dense fibrous tissue. The cut surface disclosed innumerable pockets of varying stages and sizes, the largest being about one-fourth inch in diameter, which were surrounded by dense fibrous tissues. These pockets contained a thick, creamy, yellowish substance. Culture of this material and that taken from other places showed us growth after forty-eight hours. The smear revealed no organ but many crystal-like bodies. This wound healed uneventfully, the patient returning for observation from time to time. About one month later there was found a very dense infiltration along the same place as where the bismuth mass was located. This did not have the same consistency nor appearance of the former mass, but was keloid in character. On this basis, radium was placed on the area. There was only a slight local reaction following this radium application but the keloid disappeared. X-rays taken since still show small bismuth plugs which could not very well be removed at operation but are evidently deeply seated.

Case 3.—Male, aged 14. This case is in practically all respects similar to Case No. 2, so that repetition will not be necessary except to say that in this instance the mass formed at the site of injection on the right side of the neck. The mass was markedly adherent to the skin, not tender and had been present for three months. It was also excised and findings were of similar nature. It is interesting to note that this boy's brother had some such similar swelling following bismuth injection but there is no confirmation of this other than clinically.

Case 4.—Female, adult. Complained of tearing and pus discharge in left eye for past year. After probing the lacrimal duct it was found to be stenotic. The patient was advised operation and so, under synergistic anesthesia, the usual incision was made and the lacrimal duct was exposed. The canaliculus had previously been injected with a 10 per cent. mixture of bismuth paste and found to be blocked about the region where it opens into the sac. The duct was then opened and the bismuth was found under tension. A dacryocystotomy was performed (all technical details of the operation being omitted). Symptoms which she formerly had subsided for a time only to reoccur again when the duct closed.

About one month later at the site of the old incision there formed a hard infiltrating mass which was not tender and not easily movable. This was thought to be due to the bismuth and roentgen ray confirmed the diagnosis. Operation was advised and so under synergistic anesthesia, the old scar was resected. It was found to be infiltrated by much of the adjacent tissue and that below it, including the anterior wall of the sac, therefore necessitating removal of the sac in small pieces. Bismuth paste was easily expressed from the meshes of this tissue. The opening into the nose was enlarged and the wound packed from within the nose, and the external wound closed completely. All went along uneventfully with ideal healing. While the patient has still some tearing, there is no more pus and no scarring resulted.

Histopathology.—The miscroscopic sections of these tumor masses show a recent, not very vascular, connective tissue in different stages of development. This connective tissue is of varying age, some dense tissue, hyaline in character, and some looser, consisting largely of fibroblasts and oval cells. Blood vessels are but few in number and show nothing particularly characteristic. Here are a great many spaces of different sizes up to a centimeter or more in diameter, irregularly distributed throughout the tissue, and in some areas are so numerous as give a honeycombed appearance. Most of the spaces appear empty, other contain bismuth granules or masses. In shape, the majority of the spaces are round or oval, the others being more or less irregular. The borders of some of the larger and irregularly shaped and slit-like spaces contain dense masses of bismuth granules, between and within the young connective tissue cells, while the smaller spaces, especially the round and oval, may be lined with a rather narrow rim of multinucleated cytoplasmic bands, resembling syncytium. Between the spaces, in the more cellular parts of the tissue, are larger and smaller multinucleated giant cells of the foreign body type, in some of which, as well as in the adjacent smaller cells may be fine bismuth granules.

The giant cells are most numerous in the region of the bismuth masses. Some are small, containing three to five oval nuclei irregularly arranged, others are larger with ten or more nuclei. Occasionally a giant cell presents a small bismuth mass within its cytoplasm.

Many of the spindle-shaped cells or fibroblasts, reveal fine and coarse bismuth granules within their cytoplasm. Some of these phagocytic cells are more oval in shape and may possibly be endothelial in origin.

A few scattered areas of round cell infiltration occur among the hyperplastic connective tissue. The cells are chiefly small lymphocytes together with a moderate number of plasma cells.

The appearance of the tissue in general is that of a granuloma, due to the irritation of a foreign body with the resulting connective tissue proliferation and giant cell formation.

CONCLUSIONS

1. Diagnostically, this type of foreign body presents another variety of a group of many and is interesting especially, since the roentgen ray shows the presence of the mass.
2. The vaseline in the bismuth paste mixture is probably responsible for the reaction.
3. The force, with which any such material as bismuth paste is introduced should be minimized.
4. Superficial structures and blind passages, especially in the presence of chronic inflammatory conditions should not be injected.
5. Bony sinuses in which the walls are not intact are contra-indicated areas.
6. That bismuth paste, is, and should be regarded as a foreign body capable of producing the same reactions as does paraffin and camphorated oil.

Nov. 13, 1922.

TWO CASES OF CONGENITAL MALFORMATION OF THE HEART VALVES

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Congenital malformations of the aortic and pulmonary valves are not common findings at postmortem examination. The malformations found are either an

increase or a decrease in the number of cusps. In a series of 15,666 reports of autopsies collected from the literature, there were nineteen instances of aortic valves with two cusps, two cases of aortic valve with four cusps; and six cases of pulmonary valve with two cusps and sixteen instances of pulmonary valves with four cusps. In another series of 10,000 autopsies seven cases of aortic valves with two cusps are mentioned and four pulmonary valves with two cusps. Four cusps in the aortic and pulmonary valves are not mentioned in this series. Hence, in 25,666 autopsies, there were twenty-six cases of aortic valves with two cusps, and ten cases of pulmonary valves with two cusps. The more common malformations of these valves are therefore, two cusps in the aortic and four cusps in the pulmonary valves. The two cases herewith reported are of these more common types.

Case 1.—This patient was a white male, aged 57 years, who died suddenly from chronic myocarditis with marked arteriosclerosis and calcification of the coronary arteries. The right heart chambers were distended with dark clotted blood, and there were subpericardial hemorrhages. The brain and lungs were edematous. The kidneys showed chronic diffuse nephritis with retention cysts in the right kidney.

The pulmonary valve is composed of four cusps; the fourth cusp is small, measures 6 mm. along its free edge, has no corpus arantii, and shows a fenestra measuring 2 mm. in diameter.

Case 2.—This patient was a white man, apparently about 50 years of age. The right heart chambers were markedly dilated and filled with dark partially clotted blood. There were subpericardial hemorrhages. The myocardium showed numerous streaks of white fibrous tissue. The coronary arteries were sclerosed. The aortic valve consists of two cusps, that are moderately thickened. These cusps are of approximately equal size, one measuring 32 mm., the other 31 mm. along their free edges. The coronary arteries come off from behind the same cusp, the right coronary being given off as two branches, 2 mm. apart, one about twice the size of the other. The left coronary artery arises only 1 mm. from the attachment of the cusp to the aorta. The distance between the mouth, the left coronary artery and that of the larger of the right, is 26 mm. On the aortic wall of the sinus of valsalva 1 cm. to the right of the opening of the left coronary artery there is a low ridge which extends to the

attached margin of the cusp, but does not extend on to the cusp itself. Each cusp shows a corpus arantii. Behind the posterior cusp (that is, the one from behind which the coronary arteries do not arise) there is a definite bulging of the aortic wall, forming a sort of "sinus aneurysm." Immediately above the free margins of the aortic cusps the aorta measures 6.5 cm. in diameter.

The extra cusp of the pulmonary valve appears to be the result of division of one of the primary cusps. Two of these cusps measure 2 cm. each along their free edges, the small cusp with its neighbor also measure together 2 cm. along their free edges. There is no thickening of the pulmonary valve, and hence no evidence that the malformation is the result of an endocarditis. It is therefore considered a true congenital malformation.

In the case of the aortic valve there is definite evidence of a chronic endocarditis, in the thickening of the two cusps. There is furthermore a ridge along the wall of the aorta between the openings of the coronary arteries which suggests the possibility of fusion of two cusps as a result of an endocarditis with later disappearance of the partition thus formed between the cusps. But there was no evidence elsewhere in the body of an ulcerative endocarditis, for there were no ancient infarcts in the kidneys or spleen. It is quite possible that the chronic endocarditis occurred postnatal, for, as pointed out and strongly emphasized by Babes, malformed valves are especially liable to the development of endocardial lesions. The location of the openings of the coronary arteries, together with the double right coronary artery, so very close to the attachment of the cusps to the wall of the aorta is strongly suggestive of some embryonic disturbance in formation of the aortic valve.

The two types of malformation herewith reported are only rarely associated with other malformations of the heart. In a series of 192 cases collected from the literature, of malformations of the aortic and pulmonary valves, 14.5 per cent. of those with two cusps in the aortic showed other malformations in the heart; 4.5 per cent. of those with four cusps in the pulmonary valve; 20 per cent. of those (five cases only) with four cusps in the aortic, and 84 per cent. of those with two cusps in the pulmonary valve showed other cardiac malformations. It thus appears that of the congenital malformations of these two valves, the type showing the

greatest number of associated malformations of the heart is that with two cusps in the pulmonary valve.

Jan. 8, 1923.

THE RELATION OF THE BOWEL TO B. COLI KIDNEY INFECTIONS

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CONCLUSIONS

1. In control dogs with normal intestines, the mesenteric glands contain bacteria in over 50 per cent. and contain B. coli in 33 per cent. of the glands examined. These facts speak conclusively for the passage of organisms from the normal bowel to the mesenteric glands.

2. Injection of large amounts of actively growing B. coli into the normal gastrointestinal tract of dogs was associated with the presence of B. coli or a B. coli-like organism in the urinary tract in three of eleven dogs. It is probable that these organisms reached the urinary tract by way of the blood stream. The lowered resistance of the animals afflicted with distemper seemed to predispose to infection of the urinary tract.

3. Moderately prolonged constipation or diarrhoea in dogs was not associated with relative increase of organisms in the mesenteric glands or with urinary tract infections.

4. Obstruction of the large bowel or traumatism of the bowel is associated with an increased bacterial content of the mesenteric glands and urinary tract infection occurred in one dog.

5. No evidence was forth coming that organisms reaching the mesenteric glands from the bowel tended to involve the urinary stream by way of the lymphatics. It is probable that Franke's hypothesis in this connection would apply only to those instances where a diseased bowel or appendix was in contact with the

peritoneum overlying the kidney. This explanation obviously would not include the great majority of kidney infections.

6. Intestinal worms seem to play a minor rôle in effecting the passage of microorganisms through the bowel.

7. Cultures of liver tissue, bile and heart's blood were uniformly sterile and lead one to believe that organisms leaving the normal intestine do so in small numbers and are at most but transient inhabitants of the blood or liver tissue.

8. The significance of the passage of intestinal organisms through normal as well as pathological bowel wall to the mesenteric glands cannot be overlooked. While it is undoubtedly true that these organisms reach the blood stream in but relatively small numbers and inconstantly, it is nevertheless possible that increased virulence of the organisms, lowered resistance of the host as well as actual lesions of the bowel wall would greatly increase this number of organisms reaching the blood stream. The conclusion would accord with the clinical relation between gastrointestinal lesions and urinary tract infections.

Dec. 11, 1922.

THE PRECIPITIN REACTION OF THYROGLOBULIN

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Thyroglobulin, first isolated by Oswald, is a comparatively constant compound in different species, except of course for variations in the iodin content. So far as we can learn the antigenic properties of thyroglobulin have not been studied, and it occurred to us that it would be of interest to do so. Accordingly we prepared thyroglobulin from beef, swine and human

thyroids in the usual way but with special efforts to obtain as pure a product as possible. The thyroids were freed from fat and connective tissue and torn into small pieces, which were washed in water until almost white and then extracted in the ice box with salt solution containing a little thymol. After filtering through paper several times the extract was precipitated with an equal quantity of concentrated ammonium sulphate solution, the precipitate washed with a 50 per cent. ammonium sulphate solution, dissolved in salt solution, and reprecipitated as before. The ammonium sulphate was removed by dialysis and the final solution given a cencentration of 0.85 per cent. sodium chloride. For injecting rabbits a 1 per cent. solution of swine and human thyroglobulin by weight was used; 10 c.c. were given intravenously every day for three days. Five days after the last injection of swine thyroglobulin, the serum of the rabbits gave a fairly strong precipitin titer, while the serum of the rabbits injected with human thyroglobulin was without any action. Beginning on the seventh day after the last injection these rabbits were given a second series of three daily injections of 10 c.c., and on the fourth day after the last injection the serum gave a very high precipitin titer. In the case of beef thyroglobulin 10 c.c. of a 1 : 250 solution were injected intravenously daily three times and on the fourth day after the last injection, the serum was found to have a good precipitin titer.

The results of the tests with the antiserums prepared as outlined are given in Table 1, the figures of which indicate the highest dilutions of the thyroglobulins and of serums with which the antiserums would form precipitates by the contact or ring method after one hour at the room temperature. In all cases in which negative results are recorded, the tests were carried through with a series of progressive dilutions of the thyroglobulin or serum in question in order to avoid the danger of being misled by failure of reaction in low dilutions of antigen due to the so-called prozone effect.

The results show that in these experiments beef and swine thyroglobulins acted as strictly specific precipitinogens, the resulting precipitin serums being

apparently specific each for the corresponding thyroglobulin, while the human thyroglobulin besides a rich output of specific precipitin, also called forth, but in far smaller quantities precipitins for swine and beef thyroglobulins and for human serum. As indicated in Table 1, the serum precipitins in the original antiserum for human thyroglobulin were removed by an equal amount of a 1 : 200 dilution of normal human serum. The precipitins in this serum for swine and beef thyroglobulin were probably of the nature of so-called minor precipitins; at any rate, mixing the antiserum with two parts of swine or beef thyroglobulin solution 1 : 3000 and removing the precipitate that formed on standing,

TITERS OF ANTITHYROGLOBULIN PRECIPITIN SERUMS

Serum of Rabbits Injected Intravenously with Beef, Human or Swine Thyroglobulin	Titers of Antiserums in					
	Beef Thyroglobulin	Beef Serum	Human Thyroglobulin	Human Serum	Swine Thyroglobulin	Swine Serum
ntibeef serums	8,000	0	0	0	0	0
ntihuman serum, original	8,000	0	1,000,000	1,600	25,000	0
ntihuman serum—after mixing with equal quantity of a 1 to 200 dilution of human serum and removing the precipitate that formed on standing	2,000	0	640,000	20	25,000	0
ntiswine serum	0	0	0	0	128,000	0
ormal rabbit serum	0	0	0	0	0	0

deprived the antiserum of all power to react with either of these thyroglobulins while it still reacted with human thyroglobulin solution at 1 : 256,000. Similar treatment of the antiserum with human thyroglobulin, on the other hand, removed all precipitins completely. Even mere dilution of the antiserum with three parts of salt solution was enough to suppress the reactions with swine and beef thyroglobulins, the titer in human thyroglobulin being reduced merely in proportion to the dilutions.

Injecting rabbits with extracts in salt solution of thyroids removed from patients with exophthalmic goiter (Dr. George W. Crile in Cleveland and Dr. J. F. Jaros in Chicago) caused the formation of precipitins for human thyroglobulin, from normal as well as

exophthalmic thyroids, and in such antiserums too minor precipitins acting on swine and beef thyroglobulins were present also.

SUMMARY

The results of this work indicate that human thyroglobulin, prepared as described, contains a main, strictly specific antigen and also lesser antigens that in the rabbit may call forth precipitins for thyroglobulins of other species. Perhaps closer study may reveal several thyroglobulins in other species also, but the beef and swine thyroglobulins used in these experiments acted as strictly specific antigens.

Dec. 11, 1922.

TISSUE CHANGES PRODUCED BY THE ACTION OF THE LIPINS OF TUBERCLE GRASS AND COLON BACILLI, AND LIVER LIPINS *

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AND

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Several investigators have reported that the materials that can be extracted from tubercle bacilli by fat solvents produce lesions resembling those of tuberculosis. Morse and Stott have produced with such extracts a fibroplastic reaction of the epithelioid type with typical cellular tubercles and characteristic giant cells. They concluded that the tubercle bacillus produces a microscopically characteristic lesion not because it is a living organism but because its waxy substances act as a peculiar type of foreign body.

* The completed article will be published in the American Review of Tuberculosis.

French observers have described the production of caseation, not only with tubercle bacillus fats, but also with similar material from the liver, and suggested that caseation depends on the action of fatty materials. We have repeated the work of previous investigators and in addition have compared the effect of the fatty materials from colon bacilli and nonpathogenic acid-fast bacteria (grass bacilli) with the reactions to preparations from tubercle bacilli and from liver tissue. The results may be summarized as follows:

Tubercle bacillus lipins and the defatted bacilli possess the power of exciting a fibroplastic reaction of epithelioid type, with tubercles, giant cells and abscesses, in the lungs and subcutaneous tissues.

Hyperplasia of the regional lymph glands was constant. Fibroplastic proliferation of epithelioid type was produced in the regional lymph glands only by the ether and chloroform-soluble lipins.

Definite epithelioid tubercles were produced only with the chloroform-soluble lipins and with the defatted bacilli. Far more definite tubercles were present in lesions induced with the defatted bacilli than in lesions induced with the chloroform-soluble lipins.

Giant cells were present in the lesions produced by injections of all the bacterial lipins tested, but were far more numerous in lesions produced by means of the defatted acid-fast bacilli.

Lipins extracted from grass bacilli and colon bacilli by similar methods produce entirely similar effects to those produced by the tubercle bacillus except that with the latter there was more involvement of the regional lymph glands. Evidently, then, the characteristic features of the tubercle cannot be considered to be a specific effect of the lipins of the tubercle bacillus, but is merely a foreign body reaction, perhaps slightly modified by the water-soluble products of the living tubercle bacilli.

Defatted tubercle bacilli and grass bacilli produce typical epithelioid cell lesions with many giant cells. Defatted colon bacilli produce similar lesions but with no giant cells.

No areas of true caseation were observed in any section. Probably the production of caseation with lipins from tubercle bacilli and beef liver reported by others depends on the solid character of the pus produced in rabbits and guinea-pigs, which macroscopically closely resembles caseous material.

It would seem, then, that the body's response to the presence of the tubercle bacillus is not a specific defense built up by the invaded organism, but merely a type defense—a reaction invoked by many and varied substances, and in no wise peculiar to tuberculous lesions. Apparently the caseation seen in actual infection with the tubercle bacillus is due to the diffusion of some toxic product of the bacillary metabolism, and is seen only when the bacilli are alive and the inflammation progressing.

Dec. 11, 1922.

TRANSACTIONS OF THE
CHICAGO PATHOLOGICAL SOCIETY

VOL. XI JUNE 1, 1923 No. 9

INVASION OF BODY BY BACTERIA FROM INTESTINAL TRACT

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SUMMARY

In our experiments with dogs, using suspensions of *B. pyocyaneus*, *B. prodigiosus* and *Streptococcus hemolyticus* introduced by stomach tube, we were unable to recover the test organisms from the chyle, blood, or organs. When bacteria were introduced into the duodenum by needle puncture, in one of the six dogs, *B. pyocyaneus* was recovered from the thoracic duct 80 and 105 minutes after injection, and similarly *B. prodigiosus* was recovered ten and sixty-five minutes after injection in one of two dogs. In these experiments, leakage from the puncture and resulting direct passage from the upper peritoneum by way of the lymphatics to the thoracic duct cannot be excluded. It should be noted, however, that the passage of organisms from the peritoneum to the thoracic duct is rapid, and such organisms usually reach the duct from this source in from five to fifteen minutes. In one of our positive results, the organisms appeared only after the lapse of an hour. Ravenel encountered a somewhat similar difficulty in his experiments, in which tubercle bacilli were injected by needle into the stomachs of young guinea-pigs. It is also possible that organisms

may have entered the lymphatics directly through the minute lesion of the intestinal wall caused by the needle puncture itself. Under ether anesthesia, movements of the intestine are decreased, and presumably the lymph flow from the intestine thereby lessened, so that under these experimental conditions the opportunity for prompt transport and consequent detection of such organisms as pass the intestinal barrier may be less than under normal conditions. Feeding experiments performed after the production of active catharsis were also negative with the test organisms used.

There seems to be no question as to the passage of certain resistant organisms, such as tubercle and anthrax bacilli, through the intact intestinal mucosa. The less resistant organisms, such as those we have used, rarely pass the intestine of healthy animals. Under conditions in which resistance to infection is decreased or when unusually hardy organisms enter the bowel, or when lesions of the bowel are present, it is reasonable to suppose that bacteria may enter the blood stream from this source.

December 11, 1922.

MULTIPLE AND BILATERAL TRAUMATIC PAROSTEAL BONE AND CALLUS FORMATIONS OF FEMURS AND LEFT INNOMINATE BONE*

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The development of parosteal bone within muscle following trauma has become an important and interesting surgical problem since the advent of the X-ray, making more certain the diagnosis of the condition and the increasing incidence of injuries due to occupation. The intense interest in this condition came about with the increasing demands made upon the

* The complete paper will be printed in Archives of Surgery.

surgeon for a more definite prognosis following injury to muscle and bone by accident insurance companies because of the workingmen's compensation law.

No attempt will be made in this paper to give a review of the literature or of various theories advanced to explain the origin of the bone. A good summary of these will be found in the papers by Josephson,[1] Cahier,[2] Schulz,[3] Jones and Morgan,[4] Macewen,[5] Painter [6] and Fay.[7]

The clinical results following an injury that lead to intramuscular bone formation are usually swelling, induration due to hemorrhage and infiltration of muscles with blood, more or less complete loss of function and usually on pressure severe pain. According to Fay,[7] page 186, "Under treatment these symptoms grow less marked, but the functional does not keep pace with the objective improvement, and the doughy mass, representing an extravasation of blood, is found to be indurated sometimes as a whole, sometimes in scattered, circumscribed areas. The impairment of function continues to increase for some weeks, and the induration becomes more marked until it is of bony hardness." According to Machol [8] these are the inevitable steps leading to ossification in uncomplicated reduced posterior dislocations of the elbow.

Clinical History.—A negro teamster, aged 44, was admitted to the Cook County Hospital, July 7, 1922, service of Dr. D. C. Strauss, complaining of pain in the lower abdomen, scrotum, penis, hips and thighs and inability to walk. He stated that Sept. 8, 1921, while loading a wagon in a gravel pit the bank caved in on him, crushing his pelvis and genitals. After the accident he lost 75 pounds and has been very weak. After the injury he was removed at once to a hospital where he was for 38 weeks. He was then taken home for 3 weeks and entered the Cook County Hospital.

1. Deutsch. militär. Ztschr. **2**: 156-161, 1874.
2. Rev. de chir. **29**: 356-367, 1904.
3. Deutsch. militär. Ztschr. **36**: 339-348.
4. Arch. Roentg. Ray **9**: 245-249, 1905; **10**: 99-100, 1906.
5. The Growth of Bone, 1912, p. 33.
6. Boston M. & S. J. **185**: 45, 1921.
7. Surg., Gynec. & Obst. **19**: 175-190, 1914.
8. Beitr. z. klin. Chir. **56**: 775, 1908.

He was a markedly emaciated colored man, temperature 98, pulse 102 and respirations 18. The pain in the lower abdomen, penis, scrotum and thighs has been present constantly since the injury, Sept. 8, 1921 and is aggravated by moving in bed. There is a deformity of the left side of the pelvis, present since the injury. The left iliac crest is rough, jagged and nodular but not tender. The left thigh swollen and hard in its upper and lateral aspect. The inability to control urinary and bowel movements dates from the time of injury. The penis and scrotum are swollen and tender and inflamed. There is marked atrophy of the muscles of the lower extremity. The left leg completely paralyzed, thigh abducted and foot rotated outward. The knee jerk and Babinski absent. The right leg can be flexed on the thigh but the muscles are markedly atrophied. The knee jerk present but Babinski absent. Died Aug 21, 1922.

The alterations found postmortem (Dr. E. R. LeCount) significant for this report are as follows:

Anatomic Diagnosis.—Parosteal bones of both femurs and left innominate bone; comminuted healed fractures of both femurs and the left innominate bone; marked generalized anemia; marked emaciation; partly dehydrated body; anasarca; edema of the brain and leptomeninges; suppurative and gangrenous balanitis; mucopurulent cystitis (urinary); ascending suppurative ureteropyelonephritis; decubital ulcers of the sacrum and both buttocks.

The bony framework of the lower extremities is asymmetrical, the left leg is 89 and the right 92 cm. long. The head of left femur is displaced from the acetabulum, the thigh is abducted and the left foot everted. The pelvis is tilted so that the left side is more caudad than the right. There is a bony hard mass of the medial and ventral surfaces of the left iliac bone, 13 cm. vertically by 6.5 side to side. There are irregular bony masses of the front of the left thigh, some attached to the femur, others free in the muscle. The entire group form a mass 10 by 10 by 9 cm. In the front of the right thigh there is a similar mass 5 by 5 by 4 cm., free in the sartorius muscle near the right anterior superior iliac spine. There is a callus of an old fracture of the upper third of the right femoral shaft 8.5 cm. vertically by 2.5 wide and elevated 0.5 cm.

On the left femur there are two masses 28 cm. above the articular surface of the knee. One is 11.5 cm. vertically, 8.5 wide and projects 6 cm. and located ventromesially; the other is cephalad, 15 cm. vertically 2 cm. wide and projects

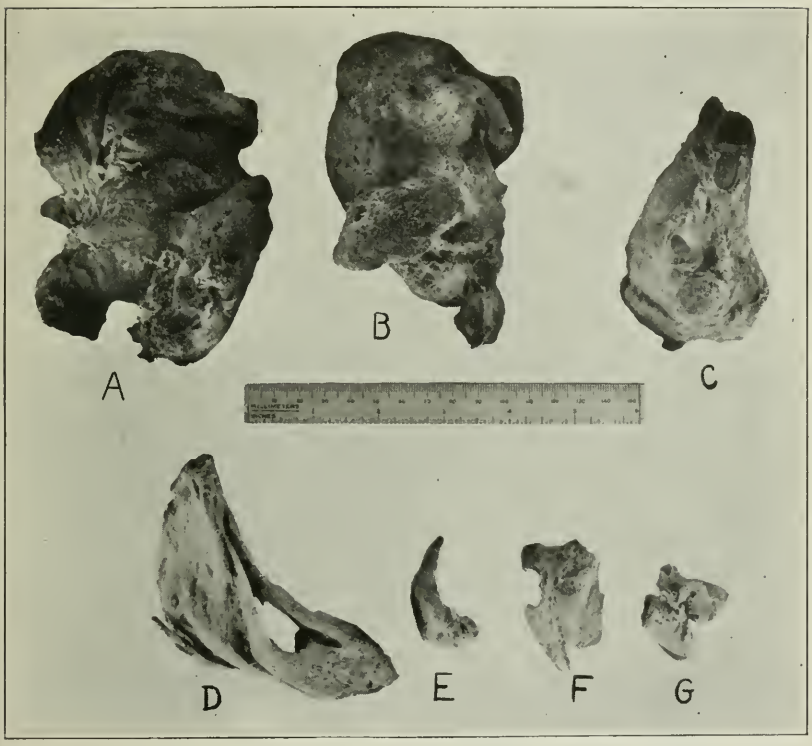

Fig. A.—Parosteal bone from left innominate bone denuded of fibrous capsule, weighs 450 gm., measures 15 by 10 by 10 cm.

Fig. B.—Parosteal bone from left femur denuded of fibrous capsule, weighs 290 gm., measures 12 by 9.5 by 7 cm.

Fig. C.—Parosteal bone from right thigh with fibrous capsule intact, weighs 100 gm., measures 8.5 by 5.5 by 4 cm.

Fig. D.—Parosteal bone from left thigh denuded of fibrous capsule, weighs 65 gm., measures 12 by 5 by 1.3 cm.

Fig. E.—Parosteal bone from left thigh denuded of fibrous capsule, weighs 5 gm., measures 4.5 by 2.5 by 1 cm.

Fig. F.—Parosteal bone from left thigh denuded of fibrous capsule, weighs 20 gm., measures 5 by 3.5 by 2.5 cm.

Fig. G.—Parosteal bone from left thigh denuded of fibrous capsule, weighs 10 gm., measures 3.5 by 2 by 1.5 cm.

ventrally 5.5 cm. The bony mass of the left anterior superior iliac region has the following dimensions: 11 by 12 by 8 cm.

On surfaces made by sawing across this last mentioned mass it is seen to project internally from the left iliac fossa. The iliac bone is clearly demarcated. Both the new bone and ileum have a corresponding texture. On a surface of the larger mass of the left femur made by sawing, two distinct parts are seen; one ventral the other dorsal and these are separated by a small amount of soft tissue into which the knife may be easily inserted. This tissue is like ordinary bone but a little more red. The head and neck of the left and right femurs, respectively, are uninjured.

Gross Anatomic Examination.—There are six irregular masses of bone from the left side and one irregular pyramidal mass from the right thigh. The two largest ones (Figs. A and B) were attached to the left innominate bone and greater trochanter of the left femur, respectively, and their projecting irregularly rounded surfaces were embedded in the muscles and fascia. The four smallest ones (Figs. D, E, F and G) were entirely embedded in the thigh muscles and had no osseous continuity with the skeleton. The largest parosteal bone (Fig. A) when stripped of muscle, fascia and fibrous capsule measures 15 by 10 by 10 cm. and weighs, Sept. 3, 1922, while still fresh, 450 gm., and in the dry condition, Oct. 16, 1922, 125 gm. The smallest piece (Fig. 5) measures 4.5 by 2.5 by 1 cm. and weighs while still fresh 5 gm. and in the dry condition 1 gm. on the respective dates cited above.

The internal arrangement of the cancellous trabeculae is clearly illustrated in surfaces produced by sawing. The intertrabecular spaces are 0.25 to 10 mm. in diameter. The trabeculae measure grossly 0.2 to 1 mm. in thickness, and although irregularly arranged, there is a tendency for them to radiate from various centers and to intersect the external surfaces of the variously rounded trabecular eminences at right angles. There is a marked deficiency of cortical compact bone in some places but in certain localities it is 0.5 to 10 mm. thick. The unattached surfaces of the largest bony mass are conspicuously cavernous or spongiform and the finer mesh work pattern is visible where the compact bone is absent.

The smaller trabecular spaces on surfaces produced by sawing and the larger, cavernous, porous places on the free surfaces of the bony masses are filled with a doughy elastic brown red vascular tissue which is easily dissected out with gentle traction. In some of the largest caverns in the bone there is a dark red friable mass like old coagulated blood.

Each mass of parosteal bone possesses a well defined connective tissue capsule with a maximal thickness of 8 mm.

There is little difficulty in denuding the bone of this capsule. It is elevated with as much ease as the periosteum of diaphyseal bone. The intramuscular fibrous epimysium as well as the intramuscular perimysium is directly continuous with this fibrous capsule.

The smallest arch-shaped specimen (Fig. E) has a diagonal groove on its concave surface which contained a gelatinous, elastic, pale red tissue 2 by 1.5 by 1 cm. and extended into the intermuscular fibrous tissue. This was dissected out, fixed in Zenkers fluid, embedded in paraffin, sectioned and stained with H. and E. for microscopic examination. Continuous with this (Fig. E) there was a projecting bony mass 3 cm. long, 2 wide, 0.5 thick, which was fixed in Zenkers fluid, decalcified, embedded in celloidin and stained with hematoxylin and eosin.

Histologic Examination.—Segments also of the parosteal bone were decalcified, sectioned and stained with hematoxylin and eosin. Sections from a number of places were studied, one place particularly is seen as a gap in (Fig. B) and in a general way they all correspond to the following description. In some places there is more bone than in others. There is slight evidence of cartilage in the center of certain bony trabeculae. The bony trabeculae are thicker close to encapsulating fibrous tissue. The trabeculae of bone vary in width up to 1 mm. There is found, in the center of certain larger trabeculae, larger lacunae with blue capsules around which the bone has grown, best seen in the narrowest and smallest trabeculae. This is absent in the thickest trabeculae. There is no evidence of inflammatory changes. Certain marrow spaces contain spindle shaped cells and loosely aggregated collections of round cells.

January 8, 1923.

PATENT DUCTUS ARTERIOSUS COMPLICATING ACUTE ANTERIOR POLIOMYELITIS

T. T. CROOKS

From the Durand Hospital of the John McCormick Institute for Infectious Diseases

Persistent patency of the ductus arteriosus over one year of age is so infrequently found that each case seems worth reporting. Wells,[1] in reviewing the liter-

1. Trans. Chicago Path. Soc. **11**: 290, 1922.

ature, finds only about twenty-five cases in adults. This case is presented not only because of the patent *Ductus botalli,* but also in the hope that the physical findings may aid in diagnosing obscure heart conditions—now conveniently classed as "congenital heart lesions"—in children.

A girl 8 years old, suffering from acute poliomyelitis, was brought into Durand Hospital, Sept. 8, 1922. The history states that she was a normal baby, had been active and healthy all of her life and had taken part in strenuous games with no signs of shortness of breath or undue fatigue.

The morning of Sept. 4, 1922, the child was unable to get out of bed because of weakness in the legs. She had a slight fever, some headache and vomited several times during the next day. The paralysis extended, and three days later she was sent to the hospital. Physical examination revealed a flaccid paralysis of the left arm, weakness of the right, and almost complete paralysis of both lower extremities with loss of all reflexes in these parts. Blood and spinal fluid examinations were compatible with poliomyelitis.

The apex heart beat was perceptible in the fourth and fifth interspaces, and the left heart border was 1.5 cm. outside of the nipple line. The heart was not enlarged upward or to the right. There was a palpable thrill over the pulmonic area and a slight systolic murmur heard over the apex but not well transmitted. Over the pulmonic area there was a harsh systolic blow and a short, soft diastolic murmur. These could be heard all over the upper chest, but were not well transmitted. The heart was rapid but regular. The beats were very forceful while the radial pulse was comparatively weak, more so on the right than on the left side. Nothing more of note was recorded.

The patient at this time seemed fairly comfortable. Three days later the paralysis had extended involving the diaphragm and intercostal muscles so that breathing became difficult and called into use the accessory muscles of respiration. The heart condition became more aggravated by the respiration difficulty, and the patient died Sept. 13, 1922. For several hours preceding death the patient was cyanotic, gasping for breath, and the heart action became weaker. With this the murmurs were less harsh, and the left heart border was 3 cm. outside the nipple line.

Necropsy showed extensive reddening of the gray matter of the spinal cord, especially in the anterior horns in the cervical part. In the midcervical region there was considerable

softening leading almost to cavity formation. The lesion gradually disappeared in the dorsal region excepting for a few small isolated red areas. In the lumbar region the grey matter was again red, but not so extensively as in the cervical region. The heart weighed 175 gm. The right ventricle was flabby and contained a considerable quantity of dark red unclotted blood. The left ventricle firm and hard; the myocardium red brown, wall 2 cm. thick. The mitral ring admitted the tip of two fingers, and the valve flaps seemed unchanged. The tricuspid ring admitted three finger tips and showed no gross changes. The semilunar valves intact and all cusps present. The aorta and pulmonary arteries showed no dilated or constricted areas. At the beginning of the descending portion of the aorta, just distal to the origin of the left subclavian artery, there was a small duct opening into the left pulmonary artery, admitting a probe about 0.5 cm. in diameter.

There are no other gross lesions of importance.

The persistent patency of the ductus arteriosus in this case evidently gave rise to no symptoms until the paralysis of respiratory muscles threw an extra load on the heart. The slight hypertrophy of the heart had evidently fully compensated for the condition previous to the onset of the poliomyelitis. With the increased strain on the heart due to respiratory failure there appeared physical findings rather difficult to explain during life, but which seemed fully cleared up by the presence of the patent ductus arteriosus.

January 8, 1923.

GASTRIC SYPHILIS—A REPORT OF TWO CASES STUDIED ANATOMICALLY

WILLIAM A. BRAMS
AND
KARL A. MEYER

Syphilis of the stomach is a rare disease from the anatomical point of view, only fourteen other reports being found in the literature in which the description

of the anatomical findings is sufficiently complete to warrant such a diagnosis. The two additional cases reported makes the total of anatomically proved cases sixteen.

The anatomical changes in the two cases are essentially:

Multiple, shallow and irregular ulcers at the pyloric end of the stomach. The striking feature on cut section of the stomach wall is the enormous thickening of the submucosa. This layer is also white, rubbery and elastic. One of the cases showed small, white, miliary gummas of this layer.

The microscopical features were a panphlebitis and panarteritis which began as a round cell infiltrate of the adventitia, extending to the other layers, finally involving the intima. Later stages showed a fibrosis of the involved layers of the blood vessels with obliteration of the lumen. The involvement of veins was especially prominent, as the endarteritis was not of a marked degree, while the veins were often completely obliterated.

A perivascular infiltrate of lymphocytes and plasma cells was also found. A diffuse round cell infiltrate formed the base of the ulcer. There were some giant cells of the Langhans type in the diffuse infiltrate. The thickening of the submucosa was caused chiefly by edema of this layer and this may have been due to the venous changes. There was not enough infiltrate and fibrosis to account for all of the thickening of the submucosa.

An outstanding finding was the presence of small accumulations of lymphocytes and plasma cells on a connective tissue framework and containing some fine capillaries. These were miliary gummas and were found chiefly in the submucosa, but some were present also in the outer muscular layer. There were no areas of necrosis or caseation.

Various stains for bacteria were made and Levaditi preparations were examined, but no bacteria or spiro-

chetes were found. The clinical history and positive Wassermann test, as well as the evidence of lues in other parts of the body, speak for the specific nature of the condition. The fact that one of the patients received antisyphilitic treatment and has remained clinically cured after resection of the lesion further supports this assumption.

The chief clinical signs were abdominal pain after meals, anacidity, history or evidence of luetic infection, and positive Wassermann tests.

January 8, 1923.

PRIMARY CARCINOMA OF MALE URETHRA

HERMAN L. KRETSCHMER

Carcinoma of the male urethra is generally considered a rare disease. In 1907 Preiswerk reported two cases and made a careful review of the literature, which at that time contained reports of forty cases, to which he added his two.

Since 1907 isolated case reports have been published, but, as far as I am aware, no extensive review of the literature has appeared. In a recent review I have been able to find reports of thirty-seven cases, but some of these were published prior to 1907 and evidently were overlooked by Preiswerk. If this number is added to the forty-two cases previously reported, the total is seventy-nine. With the case which I shall report herewith, the total number at present is eighty.

Aside from the interest in this disease, due to its rarity, the case reported is interesting because it was a papillary carcinoma, a rare type of urethral carcinoma, since the largest number hereto reported have been of the pavement or squamous-celled type. In addition to the papillary carcinoma, the entire urethra was studded with benign papillomas.

History.—Dr. N., aged 53, referred by Dr. Ralph Hissem, was admitted to the Presbyterian Hospital, Feb. 16, 1921, complaining of swelling, induration and tenderness of the shaft of the penis with fistula formation; enlarged inguinal glands; frequency and burning on urination, urgency and dribbling afterward. He had the usual diseases of childhood. No history of venereal disease. Twenty-five years previously a large mass of papilloma had been removed from the urethra with a curet.

In Nov., 1920, the patient had some irritation about the glans. There was a discharge from the urethra, perhaps due to the presence of a very long prepuce. He had similar trouble several times previously, and he had consulted a physician who advised argyrol injections, but by mistake he had used Hartzell's solution. In about an hour the prepuce became enormously swollen; the next day blood exuded from the meatus, followed several days later by swelling of the penis. Difficulty of urination occurred, and his condition became worse. An abscess formed on the inferior surface of the penis, which was lanced, Dec. 15, resulting in the formation of a urinary fistula which had been present ever since, the opening increasing in size from overgrowth of what was diagnosed at that time as granulation tissue. Numerous small abscesses had formed since, causing multiple fistulas. Acute retention occurred about the middle of December, at which time Dr. Hissem made a dorsal slit in order to expose the meatus. The penis was swollen to the size of the patient's forearm. He had fever, toxemia and extravasation of urine. Sounds up to No. 31 were passed under ether, and an indwelling catheter was inserted for four days. The bladder was irrigated because of pus, and sounds were passed every two to three days. The large sizes produced bleeding.

It was never noticed that the inguinal glands were enlarged until the last few days before admission. They were never tender. There was no hematuria, epididymitis or backache.

Examination of the heart and lungs was negative. Neither tenderness nor masses were discovered in the abdomen.

Examination of the testicles was negative; the spermatic cords were tender but not enlarged. The inguinal glands on both sides were enlarged and slightly tender. The penis was greatly enlarged, being 7 cm. in diameter and about 20 cm. in length. On the lower surface, about the middle, was a mass of red granulation tissue, 3.5 cm. in diameter. Beside it was a fistula, 1 cm. in diameter. The urine flowed through this

mass. The shaft was hard, not very tender and moderately reddened, and the induration extended down to the symphysis and then stopped. Posteriorly, it could be felt extending to the perineum. The prepuce was very thick. Pus was present at the meatus.

The prostate was small and soft, and the seminal vesicles were palpable.

Leucocytes numbered 10,300; hemoglobin, 69 per cent. Blood pressure systolic, 155; diastolic, 84. Wassermann reaction, negative.

Feb. 26, 1921, under ether anesthesia, amputation of the penis, transplantation of the urethra into the perineum and removal of the inguinal glands en masse were carried out. The first step in the operation was the removal of the inguinal glands. The patient made an uneventful recovery.

The pieces removed from the large tumor showed papillary carcinoma. Six different sections from six different glands revealed no evidence of carcinomatous infiltration. The glands were filled with large numbers of round cells. The diagnosis was chronic adenitis.

The patient died, Aug. 22, 1922.

Primary carcinoma of the male urethra may be classified as follows: (1) Squamous-cell carcinoma; (2) columnar-cell carcinoma; (3) papillary carcinoma, and (4) adenocarcinoma.

The squamous-cell carcinoma is by far the most frequent type of carcinoma in the urethra. In Preiswerk's tabulation of 39 cases, 31 belonged to this group. In the 36 cases collected in this review, 24 were of this type. Perhaps the total number of the squamous-cell type is even higher, since in some of the case reports a diagnosis of carcinoma was made without stating the type of the cells. Normally, the prostatic urethra is lined with transitional epithelium and the penile urethra with columnar epithelium, only the fossa navicularis having squamous epithelium. The development of a squamous-cell carcinoma of the penile urethra can be explained on the basis of metaplasia, as a result of which patches of leukoplakia form, which then undergo malignant degeneration. In the same manner, squamous-cell carcinomas occurring in other parts of the other urinary organs (in parts which do not nor-

mally contain squamous cells), such as the kidney pelvis and the urinary bladder, can be explained.

Columnar-cell carcinomas are quite rare. Only one of Preiswerk's collected cases belonged to this type, the one reported by Cabot. Of the cases in this series, none was columnar-cell carcinoma.

The papillary carcinoma is as rare as the columnar-cell variety. Preiswerk included only one case of this type (Buday). Subsequently, cases of this type were reported by English.

The case reported now showed, besides a large papillary carcinoma, many benign papillomas. It may be stated with reason that one of the previously benign tumors had undergone malignant change, a somewhat analogous condition occurring in certain bladder tumors.

When adenocarcinoma is found, the consensus of opinion is that its source is most frequently in Cowper's glands; hence this type has been considered as primary in Cowper's glands with secondary invasion of the urethra. In rare instances, it may happen that the tumor originates in some of the urethral glands, in which case it would be classified as a true adenocarcinoma.

The carcinoma may spread along the mucous membrane of the urethra. As the tumor enlarges, the lumen of the urethra is encroached upon and the symptoms of stricture supervene. At times it extends into the spongy bodies, and not infrequently grows outward so that a palpable mass is present. Infection is a concomitant of the tumor; hence suppuration ensues and the clinical picture is that of a periurethral abscess. Later fistulas may form, with escape of urine through the fistulous opening. In the course of the disease there is an early involvement of the inguinal glands, record of which involvement has been stated in fifteen cases. In one case involvement of the lumbar glands was found at necropsy (Montgomery).

February 12, 1923.

The full paper was published in detail in Archives of Surgery, May, 1923.

CONGENITAL HYPOPLASIA OF LEFT VENTRICLE AND OF ROOT AND ARCH OF AORTA

J. LISLE WILLIAMS

From the Pathological Laboratory of the Evanston Hospital, Evanston, Ill.

This specimen was removed during the postmortem examination of a white girl child 4 days old, on the service of Dr. Schneider, born after a normal labor of ten hours, and weighing 7 pounds. Two days later twitching and oscillatory movement of the arms were noticed. There was a loud systolic murmur heard most distinctly at the base of the heart. The lips were cyanotic and the anterior fontanelle bulged slightly. During the third day there was slight improvement, but subsequently the child became very cyanotic. She was unable to nurse, the respirations were shallow, irregular and rapid. Examination on the fourth day disclosed a distended abdomen, an enlarged liver and an internal strabismus. Rapidly she became worse, went into coma and died.

Among the chief pathological changes noted were congenital hypoplasia of the left ventricle and of the root and arch of the aorta; huge dilatation of the right auricle; marked hypertrophy of the right ventricle; dilated and enlarged ductus arteriosus; marked passive hyperemia of the lungs, liver, kidneys and spleen; slight ascites; slight edema of the mediastinum, back of the trunk and lower extremities; anomalous origin of the right coronary artery; congenitally absent left coronary artery, and slight generalized icterus.

A detailed description of the heart follows:

As it lies in the chest the heart is greatly enlarged and is 6.5 by 5.0 by 4.5 cm. The right auricle is greatly distended and comprises approximately three fourths of the volume of the organ. The myocardium of the right ventricle averages 0.8 cm. thick. The pulmonary artery is dilated. The ductus arteriosus is 1.4 cm. in circumference; its wall is thickened; its lining thrown up into folds. The cavity of the right ventricle is enlarged with numerous recesses extending among

the papillary muscles and columna carneae. The wall of the right auricle is thin, its fibers distinct. The foramen ovale is a narrow slit 0.8 cm. long. The left auricle is poorly developed, its appendage small and contracted. A narrow ridge of tissue extends from the posterior margin of this foramen into the left auricle as if to deflect the blood from the pulmonary veins into the right auricle. The mitral orifice is barely patent. At the usual site of the mitral cusps two thin membranous leaflets separate the left auricle from a rudimentary left ventricle whose cavity is less than 0.5 cm. in diameter. There is no direct connection between this minute pouch and the cavity of the right ventricle or the lumen of the aorta. The aorta begins as a continuation of the ductus arteriosus and has no root or arch such as seen in a normal aorta. Two main branches arise from the beginning of the aorta, one going to the left side as the subclavian artery, the other to the right. From this right branch the left common carotid and the innominate artery arise. The single coronary artery arises from the innominate branch on the right side.

The blood of the lesser circulation in this heart must have joined that of the greater by returning to the right auricle through the foramen ovale, i. e., reversing the flow during fetal life. Hence the heart functioned as a two-chambered organ or cor biloculare—the left auricle serving merely as a channel from the lungs to the right auricle, a condition somewhat analogous to that in the fish. This developmental defect is probably a result of the misplacement of the interventricular septum to the left in embryonic life thus causing a hypoplastic left ventricle to develop.

The absence of the interventricular septum, according to Thomson [1] and Osler,[2] is not infrequent in congenital defects of the myocardium. The absence of the aortic ring and of the root and arch of the aorta is believed by Keith [3] to be of rare occurrence. Abbott [4] does not include such an anomaly in her comprehensive classification of congenital cardiac malformations.

Feb. 12, 1923.

1. Oxford Medicine, **2**: 371-386.
2. Principles and Practice of Medicine, 1916, pp. 832-836.
3. Lancet **2**: 356, 433, 519, 1909.
4. Modern Medicine **4**: 323, 1915.

AN ANALYSIS OF 545 CASES OF MALIGNANT NEOPLASM OBSERVED AT POSTMORTEM EXAMINATION

WITH REFERENCE TO THE RELATION OF CLINICAL AND ANATOMICAL DIAGNOSIS

H. GIDEON WELLS

Although it is generally recognized that vital statistics of cancer contain a serious error because of the frequency with which internal cancers are unrecognized during life, we have but little actual evidence as to the true facts. I have, therefore, gone over the available autopsy records of the Cook County Hospital for the years 1917-1922, inclusive, comprising about 2,712 autopsies, and also 1,000 other records of my own

TABLE 1

	Cook County Hospital	University of Chicago	Total	Per Cent.
1. Correctly diagnosed as malignant tumors...	257	110	367	67.34
2. Not recognized as malignant tumors.....	125	53	178	32.66
	382	163	545	100.00

autopsies not included in these statistics, although many of them were performed in the Cook County Hospital at an earlier date than 1917. In these 3,712 autopsies were disclosed 545 cases of malignant disease, or 14.7 per cent. In our figures are included all forms of malignant tumor, as well as cerebral gliomas and endotheliomas, that were met with on the autopsy table.

To offset this large error of omission, we find errors of commission, i. e., cancer diagnosed as present when no malignancy was found at autopsy, there being 23 such in the county hospital figures and 10 in the University of Chicago figures, making a total of 33 to be subtracted from the 178 cases erroneously added. Therefore, our autopsies added to the 400 cases diagnosed cancer during life (367 correctly and 33 incorrectly), 145 cases, or 36 per cent.

When we tabulate our cases we find that an excessively small proportion are in sites accessible to direct examination. Divided on this basis, we have the following results:

TABLE 2

	Cook County Hospital	University of Chicago	Total	Per Cent.
1. External* tumors correctly diagnosed....	61	21	82	89
2. External tumors not recognized	5	5	10	11
3. Internal tumors correctly diagnosed....	196	89	285	62.9
4. Internal tumors not recognized	120	48	168	37.1

* Under external tumors are included carcinomas of the skin, mouth, tongue, pharynx, breast, uterus, penis, sarcomas of the extremities or superficial structures, but not carcinomas of the rectum, bladder or larynx.

The error in diagnosis of internal tumors, 37.1 per cent., was almost exactly the same as reported for inaccessible tumors in the London hospitals, 37.3 per cent.

Full details of the statistics, with consideration of the errors in diagnosis and also the different distribution of tumors in respect to organs and histological structure, will be found in the complete article published in the *Journal of the American Medical Association.* 80:737-740 (1923.)

Feb. 12, 1923.

PRECIPITATION TEST FOR SYPHILIS OF SPINAL FLUIDS

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From the John McCormick Institute for Infectious Diseases

The ring or contact method of precipitation for syphilis as made with serums was found less sensitive than the Wassermann test when applied in a similar way to spinal fluids.

The globulins after precipitation with saturated solution of ammonium sulphate can be redissolved in normal saline solution in a quantity equal to a fractional amount of the original fluid. As the globulins were found to contain the syphilitic antibodies, it was possible to get a concentration ten to fifteen times greater than in the original fluid. Consistent results were then obtained when precipitation and Wassermann reactions were compared.

An experiment with pooled syphilitic spinal fluids and varying quantities of saturated solution of ammonium sulphate indicated that the best results were found when 3 c.c. of spinal fluid was mixed with 2 c.c. of saturated solution of ammonium sulphate. The centrifugaled precipitate was redissolved in 0.2 to 0.3 c.c. of normal salt solution, which was then tested with cholesterilized antigen after dilution to 1 to 10 with normal salt solution. This method was applied in a series of 128 routine tests.

The precipitation results in this series agreed very closely with the Wassermann reaction as made on the whole fluids. The concentrated globulin of streptococcic and meningococcic spinal fluids give negative tests with cholesterilized antigen.

This is a simple method of precipitation and the results indicate that it is a valuable check on the Wassermann test of spinal fluids.

March 12, 1923.

BACILLUS ENTERITIDIS PERITONITIS, WITH REPORT OF A CASE

ALLEN A. C. NICKEL

From the Pathological Laboratories of Rush Medical College and St. Luke's Hospital

Although infections with *Bacillus enteritidis* are not uncommon, descriptions of the tissue changes accompanying them are infrequent. Many instances of poisoning by food, contaminated with *Bacillus enteriti-*

dis, are reported from England and central Europe, whereas the number from America is not large.

Since Gaertner's discovery of this organism in 1888 as the cause of a dysentery epidemic, many other instances of similar food infections have been reported, and in 1913 they were summarized by Savage.[1] Excluding the cases previous to 1890 because of inadequate investigation and bacteriological methods, his summary includes 4,500 patients, of which 91, or approximately 2 per cent., died. However, of these 4,500, the illness in only 1,072, with 21 deaths, can be definitely ascribed to *Bacillus enteritidis;* in other words, only 16 of the 105 epidemics recorded after 1890 are known, without doubt, to have been due to *Bacillus enteritidis.* The remainder were caused by other bacteria of the Gaertner bacillus group including *Bacillus suipestifer, Bacillus paratyphosus B* and *Bacillus morbificans bovis.* There may have been a few infections included in this summary which were mixed with *Bacillus enteritidis.* The number of infections since 1913 is estimated to be approximately as great as prior to 1913.

The *Bacillus enteritidis* is, however, no longer, considered as a single organism, but is rather regarded as a group of closely related organisms. Gruschka [2] carefully studied four Gaertner strains, and observed variations in the cultural qualities with each. Some of the organisms reverted back to the main type, in others the variations remained constant. Jordan [3] says, "Considering all the evidence, there seems no escape from the conclusion that variations both in nature and in artificial test tube cultures are exceedingly common throughout the para typhoid-enteritidis group."

Before the late world war, attempts were made to classify the various forms of typhoid enteritis into three clinical groups: (*a*) the gastrointestinal, (*b*) the typhoid and (*c*) the choleriform. Research during and since the war has shown that these three clinical forms

1. Reports to the Local Government Board (Great Britain) on Bacterial Food Poisoning and Food Infection, Food Reports, London, 1913, No. 18.
2. Wien. klin. Wchnschr. **33**: 964, 1920.
3. Jour. Infect. Dis. **26**: 427, 1920.

are inadequate. In 1918 Loele [4] described, in addition to the usual forms, a septic form, a bronchopneumonic form and a rheumatoid form. During this period new strains of the colon-typhoid group of bacteria have been described, such as the Glässer-Veldagsen bacillus which is similar to the *Bacillus suipestifer*, and the Flugge-Krusche bacillus or *Bacillus enteritidis* of Breslau (according to the Kiel school) described by Shittenhelm [5] as distinct from the generally known *Bacillus enteritidis*. During the war it was also noted that dysentery was caused by paratyphus B as well as by other bacteria of the colon-typhoid group, and attempts were made to differentiate the dysentery-like ulcer from the typhoid ulceration. Shittenhelm [5] states that the differentiation clinically between an infection by *Bacillus enteritidis* and one by *Bacillus paratyphosus B* is made by the typical typhoid nature, the milder course and the more acute onset of the latter. On the other hand Neffer, Dopper and Kathe [6] report a typical typhoid infection clinically and the first doubt of a *Bacillus paratyphosus* infection was aroused when the blood serum of the patient failed to agglutinate the paratyphoid bacillus.

Because of such observations, Breitzke [7] doubts whether infections with *Bacillus enteritidis* are pathologically distinct from infections with *Bacillus paratyphosus*, or from any other acute intestinal infection. Posse [7] reports the changes found post mortem with a fatal infection with *Bacillus enteritidis* and concludes that there are no characteristic alterations, and that the clinical, anatomic and bacteriological data are necessary to decide. In other words, the changes caused by each of the two organisms are so much alike that a definite diagnosis cannot be made on the tissue changes alone.

Most infections with Bacillus enteritidis are due to the ingestion of raw or poorly-cooked, infected meat. Other food may also be important for Aumann [6] reports an instance of poisoning from chocolate pud-

4. Lubarsch-Ostertag's Ergebnisse **18**: 546, 1915.
5. München. med. Wchnschr. **67**: 1309, 1920.
6. Uhlenhuth-Hübener in Kolle-Wassermann: Handbuch der pathogenen Microorganismen **3**: 1107, 1914.
7. Cited by Posse, C. B.: Virchow's Archiv. **237**: 380, 1922.

ding; Bofinger and Dieterlen [6] report two from potato salad and Rosenau and Weiss [8] describe an epidemic in Washington, D. C., spread by infected bread pudding. However more than 80 per cent. of the infections recorded in the literature have resulted from meat poisoning. The meat is not necessarily putrid. Repeatedly the meat has not had any unnatural odor or taste nor was it discolored; in fact, usually the meat seemed clean in all respects. The only suggestive features noted have been excessive moisture combined with exposure, both favoring growth of bacteria in it.

Heredity, age, race, sex, occupation, etc., play little part, if any at all, as causes predisposing to infection with *Bacillus enteritidis*. Individual resistance naturally does play a part and the season also, inasmuch as warmth hastens the growth of bacteria in the food. Infections with *Bacillus enteritidis* have an incubation period of a few hours to one or two days. Sometimes the sypmptoms have started as late as eight days after the eating of the infected food. The onset is sudden, accompanied by nausea, vomiting, sweating, great weakness, diarrhea and organ and body pains. The abdomen becomes sunken and tense, the blood pressure low and the pulse weak. The bacillus can be found in the stools from four to six days after the onset. Later there is marked thirst and the body becomes markedly dehydrated. The stools are generally green, liquid and offensive. There is generally no edema, no palpable liver or spleen. There is an increase of the leukocytes of the blood and the urine contains albumin. Shittenhelm [5] states that there is a rapid rise of temperature of about four degrees at the beginning and then a drop, and that if the infection is severe, the temperature becomes subnormal. The duration of the disease is from two to three or ten days. If fatal, death usually occurs within a week, and in some fulminating cases it may occur within twenty-four hours.

Bacillus enteritidis is pathogenic not only for man but also in cattle and monkeys. Sherwood [9] fed non-lactose fermenting organisms, similar to *Bacillus*

8. J. A. M. A. **77**: 1948, 1921.
9. Abstracts of Bacteriology **4**: 9, 1920.

enteritidis, to two monkeys, and one became sick after ten days, had a fever of 1 to 2½ degrees Fahrenheit and a diarrhea for three days. The other monkey died and *Bacillus enteritidis* was obtained from the small bowel and lungs. The anatomic diagnosis at necropsy was ileo-colitis, mucopurulent bronchitis, bronchopneumonia with marked edema and emphysema of the lungs. The *Bacillus enteritidis* is also pathogenic in sheep, pigeons, goats and chickens. Cannon [10] reports many instances of infection among laboratory rodents (kind not stated) and with all there was a diarrhea, blood in the bowel with prominent Peyer's patches, an enlarged spleen and focal necrosis of the liver. We have the following case to report:

Clinical History.—Man, white, aged 38 years, entered the Cook County Hospital, July 21, 1921, service of Dr. Williamson, complaining of pain of a constant dull type with no radiation, in the epigastrium and right hypochondrium; and stated that he had vomited twelve times in three days, the vomitus being very bitter and yellow to green; that he had a watery diarrhea with ten to fifteen stools per day and a constant headache of frontal origin; and that the pains in the epigastrium caused him to double up and groan and seemed like a "ball of fire." He also stated that he had been drinking water from a pump at a suburb of Chicago and knew of twenty-five other men who had been drinking from the same well for some time and had similar symptoms. The patient's sister stated that where he worked it was hot and that after drinking the water he became sick, vomited, had a diarrhea and chills. "His legs gave way under him and everything went black." Another person stated that the men who were working there ate green apples and pears from an orchard, and that "several of them had abdominal pains and cramps but all of them except M. H. recovered."

He had a diarrhea for two days about three weeks before entering the hospital, another attack for four days about a week later and the last attack which began on July 19 with pain, vomiting and diarrhea; and which started suddenly while at work and constantly grew worse. On entrance to the hospital his pulse rate was 94, his respirations were 22 per minute and his temperature was 98.2 F. His pulse was feeble, expression anxious and his extremities were cold. There was a diffuse tenderness over the whole abdomen

10. Jour. Infect. Dis. **26**: 402, 1920.

especially on the right side and the white cell count was 8,400. The urine repeatedly contained leukocytes, epithelial cells and hyaline casts. He gradually grew worse and death occurred July 25 at 8 p. m., approximately four days after entrance to the hospital.

Postmortem Examination (Dr. E. R. LeCount).—Only details pertinent to the infection are mentioned here. There was a peritonitis with masses of fibrin and purple discoloration of the bowel in places. The bowel was heavy with fluid in it. There was no gross change of the colon except passive hyperemia. At the eleocecal valve there was a sharp line of demarcation between the lining of the ileum and that of the cecum, for the former was red with dark petechial hemorrhages and the tips of the rugae of the distal 30 cm. of the ileum were grey to black from necrosis. There were no visible Peyer's patches or lymph follicles but the lining was roughened by firm granules about 1 mm. in diameter. The changes became less marked more proximally so that the lining was less granular and only occasionally were the tips of the rugae grey. About 2 meters from the ileocecal valve however, the appearance of the ileum was exactly like that described close to the valve and the rugae here were extremely necrotic. This extended for 180 cm. and proximally to this the lining gradually became uniformly pink with pin-point petechial hemorrhages, and this extended all the way to the duodenojejunal junction. The bowel was everywhere distended with yellow-brown fluid. The duodenum and stomach were unchanged except for petechial hemorrhages and hyperemia. The spleen was soft and dark blue with no visible malpighian corpuscles and it weighed only 128 gm. The liver was very slightly nodular and appeared finely granular, cutting with slightly increased resistance. The parenchyma was pale yellow-brown with faint irregular lobule markings and mottled with fibrous tissue.

Histology.—In sections of the ileum and jejunum there is a superficial necrosis of the mucosa, most marked at the tips of the villi where practically all of the glandular structure has been destroyed. The tips are widened and infiltrated with blood, necrotic material and round cells. The round cells extend throughout the submucosa and into the deep fascia. There are many scattered mononuclear cells and the sections are mottled about one-thirtieth with small patches of fibrin. The muscularis mucosa is quite well preserved.

In sections of the spleen there is a good deal of intracellular blood pigmentation, the malpighian bodies are small and the capsule is wrinkled. The convoluted tubules of the

kidneys are swollen. The glomeruli fill the capsule well and the intima of the larger arterioles is slightly thickened. In addition to coal dust and a slight thickening of the lining of the arteries, sections of the lung contain distended blood vessels, and some alveoli a good deal of blood with an occasional leukocyte and some mononuclears. In some places in the alveoli there are quite a few lymphocytes. In sections of the adrenals and testes, nothing of importance is noted. A moderate amount of hemachromatosis is present in the pancreas and liver.

In sections stained for bacteria, there are a few scattered

		Bacterium				
Mediums	Incubation Period	Mucosus Capsulatus	Coli-communior	Enteritidis	From Lymph Gland	From Spleen
Milk.....	24 hr.	sl. acid	str. acid	sl. acid	sl. acid	sl. acid
	48 hr.	ac. & coag.	ac. & coag.	alkaline	alkaline	alkaline
	7 da.	ac. & coag.	ac. & coag.	alkaline	alkaline	alkaline
Dextrose.	24 hr.	acid	ac. & gas	ac. & gas	ac. & gas	acid
	48 hr.	acid	ac. & gas	ac. & gas	ac. & gas	ac. & gas
	7 da.	acid	ac. & gas	ac. & gas	ac. & gas	ac. & gas
Lactose..	24 hr.	sl. acid	sl. acid	sl. acid	nil.	sl. acid
	48 hr.	neutral	sl. acid	sl. acid	nil.	sl. acid
	7 da.	neutral	sl. acid	acid	nil.	sl. acid
Saccharose	24 hr.	ac. & gas	ac. & gas	nil.	nil.	nil.
	48 hr.	ac. & gas	ac. & gas	nil.	nil.	nil.
	7 da.	ac. & gas	ac. & gas	sl. acid	nil.	nil.
Inulin....	24 hr.	sl. acid	ac. & gas	nil.	nil.	nil.
	48 hr.	sl. acid	ac. & gas	nil.	nil.	nil.
	7 da.	ac. & gas	ac. & gas	nil.	nil.	nil.
Maltose..	24 hr.	acid	ac. & gas	ac. & gas	sl. acid	nil.
	3 da.	acid	ac. & gas	ac. & gas	ac. & gas	nil.
Salicin...	24 hr.	acid	nil.	decolorized	nil.	decolorized
	3 da.	acid	nil.	decolorized	nil.	decolorized
Mannite..	24 hr.	acid	nil.	decolorized	ac. & gas	decolorized
	3 da.	acid	nil.	decolorized	ac. & gas	decolorized

bacilli in the superficial layers of the intestinal mucosa and spleen, adherent to clumps of necrotic cells, but no such prominent clumps as reported by Posse.[7]

Cultures were taken from various parts of the body and direct smears revealed only a few scattered cocci, but a great abundance of gram negative bacilli. Culturing in the usual method, the cocci were found to be *Staphylococcus albus*. At times the bacillus seemed to be encapsulated and at other times it seemed quite motile. With a modified flagella stain, flagella could be seen quite easily. When young, the organism was motile, but it seemed to lose its motility in from seven to ten days. This organism, when injected into a rabbit, caused its death in ten days. At necropsy there was an acute hemorrhagic enteritis and the same organism was recovered in pure culture and seemed to be even more virulent.

Two strains of the bacterium, responsible for this fatal infection, one from a lymph gland, the other from the spleen of the inoculated rabbit, were grown simultaneously with a *Bacillus mucosus capsulatus*, a *Bacillus coli-communior* and a *Bacillus enteritidis*, all from "standard" and carefully kept stock, with the results shown in the accompanying table.

To identify more closely this unknown bacillus, recovered again from the body of a rabbit, with the *Bacillus enteritidis* group, two known strains of *Bacillus enteritidis* were obtained from "standard" and reliable sources and immune serums prepared in rabbits, with each of the three. Cross agglutination tests established the identity of the unknown strain with the two known *Bacillus enteritidis* strains.

CONCLUSIONS

(1) This report concerns a death with enteritis and peritonitis due to *Bacillus enteritidis*, (2) The causative bacterium was isolated from the blood and different parts of the body at necropsy, and (3) The alterations due to the infection are described.

March 12, 1923

CARCINOMA OF THE ESOPHAGUS PERFORATING INTO THE TRACHEA

SIDNEY A. PORTIS

It is because of two interesting points that I am presenting this tumor to you. In the literature on carcinoma of the esophagus it is stated that 50 per cent. of the tumors perforate either into the trachea or bronchi.

This patient, male, aged 54, was referred for diagnosis by Dr. Alfred Strauss, Sept. 5, 1922. He complained of dysphagia, weakness, spots before the eyes and nervousness. The onset was acute, four weeks before, after swallowing some solid food. Since then solid food seemed to cause distress, but chopped or liquid foods none. There was no nausea, no regurgitation. He was slightly weaker. He lost a few pounds, was nervous and easily excited. He had no cough, no night sweats, or no afternoon fever. The bowels were constipated, appetite good, no nocturia. He was active, slept well, used coffee and alcohol moderately, but tobacco exces-

sively. His wife and two children were living and well. There were no tuberculosis nor cancer in the family. Thirty years before had had a soft chancre, but no secondaries. Denied gonococcal infection. He had had no other previous illnesses.

He did not look acutely ill. The thyroid was slightly enlarged, he had a fine tremor of the hands and tongue, and a distinct eye muscle disturbance. Von Graeffe positive. Pupils reacted normally. Reflexes were slightly exaggerated. The lungs were normal. There was a slight systolic murmur heard best over the base of the heart. The blood pressure measured 140 systolic and 70 diastolic. He was slightly tender in the region of the gallbladder, but more so in the sigmoid region. The remainder of the abdomen was negative. The epitrochlears were slightly palpable. The urine showed a faint trace of albumen but otherwise was negative. The stool did not show any occult blood. No stomach test was made, for fear of traumatizing the esophagus. Blood count was normal except for a slight polymorphonuclear leukocytosis. The Wassermann test was negative.

The x-ray revealed normal lungs. The aorta showed a marked bowing of the arch, which extended into the posterior mediastinal space. There was a small calcified mass in this region, just in front of the esophagus. The heart was not enlarged. The thick esophageal paste showed a distinct delay in its passage through the upper portion of the esophagus, and when patient was in oblique position there was a distinct irregular concavity of the shadow here. When patient was in opposite oblique position there was a distinct irregularity seen just below the part of constriction. There was no marked dilatation above. The stomach was negative. The duodenal bulb was negative. The twelve hour bismuth meal was massed in the ascending and transverse colon. The rest of the colon was moderately spastic. There was no tenderness over the appendix. The appendix was not seen. There was no tenderness over the region of the gallbladder.

September 15 the patient was esophagoscoped, and the instrument met with an obstruction about 10 inches below the teeth. It was circumscribed. The esophagus was edematous and thickened here. He entered Michael Reese Hospital, September 21, a gastrostomy was performed the following day, and a silk thread which had been previously swallowed was brought through this opening. September 27 he was given 1,275 milligram element hours of radium inserted by means of the fluoroscope, and this was followed by deep

roentgen-ray therapy, and shortly afterward patient went home. He continued to feel well and gained in weight, although no food was allowed to be swallowed, the patient being fed through the gastrostomy since operation.

He re-entered the hospital on November 7 and on November 8 radium was again inserted, followed by similar roentgen-ray therapy. Patient was discharged November 14.

Shortly afterward he began to cough and had a marked hoarseness. A paralysis of the vocal cords was found. He continued to have a paroxysmal cough, and re-entered the hospital, December 7. December 10 at 6:30 p. m. he had a severe chill, so severe that he shook the bed, and his temperature rose rapidly to 104.2. The pulse was 140 and respirations 36. A diagnosis of aspiration embolus was made, although no definite dulness was found in the chest. There were scattered moist râles over the right lower lobe. The patient subsequently developed all the physical signs of a consolidation of the right lower lobe, and the temperature remained septic in character, although many times it was normal, but rose frequently to as high as 102 and 103. He became markedly anemic and emaciated, and died on Jan. 9, 1923.

The necropsy, one and one-half hours after death, by Dr. Bernard Portis revealed the following essential lesions:

The abdominal cavity is free from fluid. The stomach is densely adherent to the anterior abdominal wall in the region of the gastrostomy. The appendix is free but retrocecal. There are adhesions about the lower pole of the spleen, and about the gallbladder.

The left pleural cavity is partially obliterated by firm, fibrous adhesions over the lateral and posterior aspect. The right pleural cavity is normally free. The right lower lobe is completely consolidated. The cut surfaces reveal a uniform dense reddish tissue with numerous slightly elevated grayish areas of about 0.5 to 1 cm. in diameter. The tissue within these areas appears somewhat necrotic and has a foul odor.

The upper and middle lobes are edematous and partially consolidated, similar to the lower lobes. The left lower lobe is partially consolidated, resembling the right lower lobe. The remainder of the left lung is edematous. There is extensive bullous marginal emphysema of both lungs.

The trachea contains a hemorrhagic purulent exudate on its surface. At the point of bifurcation of the trachea into the two larger bronchi there is an erosion of the posterior wall, 3 by 2 cm. The ulceration leads directly into the esophagus, and a finger tip can be readily passed through from one to the other. The upper third of the esophagus is

somewhat thick, but of normal appearance. Beginning at 2 cm. above the bifurcation of the trachea there is an ulcerating tumor which completely replaces the normal esophageal wall for 7 cm. This mass measured 7 by 4 by 2.5 cm. At its middle point there is the perforation into the trachea just described. The esophagus below the tumor is normal.

The peribronchial and peritracheal lymph glands are somewhat enlarged and anthracotic, but there is no definite evidence of tumor.

The pericardial cavity is free, myocardium pale, valves normal, as is the aorta.

The stomach is normal except for the gastrostomy wound. The liver is normal and shows no evidence of metastatic growths.

The gallbladder is bound down by adhesions, no stones. The kidneys are somewhat increased in size, cut surface shows cloudy swelling. The spleen is normal as is the pancreas.

Miscroscopic Examination.—The lungs reveal patches of pneumonic consolidation with infiltration of fibrin and leukocytes into the alveolar spaces. In addition there is quite extensive necrosis of the pulmonary parenchyma and in these regions there are large accumulations of bacteria. In many portions the patches of consolidation tend to be confluent. In other places there is an extensive edema of the lung and a proliferation of phagocytic cells. There is no evidence of metastases within the lung.

Section through the tumor in the esophagus reveals a typical squamous cell carcinoma in which the cells show a marked variation. There are many abnormal mitotic figures. Many of these cells have undergone vacuolation and pycnosis, probably due to radio-activity. The peribronchial and supraclavicular glands reveal only a diffuse hyperplasis and edema of the stroma, and there is no evidence of metastatic growths. Sections of other portions of the esophagus in the region of the tumor show, in some places there is an extensive necrosis, in others a proliferation of hyalinized connective tissue. It is interesting to note that there is comparatively little malignant tissue remaining, and much of the tissue that is present has undergone retrogressive changes.

The points of interest in this case are: First. The comparatively little malignant tissue left, and much that present has undergone retrogressive changes. It seems likely that the perforation of the esophagus into

the trachea in this particular case may have been due to necrosis and ulceration induced by the radium. It is probable that the radium was given in too large doses, or that there was a marked susceptibility of that tissue to radium. Very shortly before the perforation occurred there occurred paralysis of the vocal chords, due, in all probability, to the effects of the radium. The fact that the tumor itself was not a very extensive one leads one to believe that the radium, as far as the tumor cells were concerned, had rather marked effects.

March 12, 1923.

SARCOCARCINOMA OF THE UTERUS

RICHARD H. JAFFÉ

From the Department of Pathology, University of Illinois, Medical School, and the Uihlein Memorial Laboratory of the Grant Hospital of Chicago

The question whether there exist tumors representing a real combination of sarcoma and carcinoma is not yet settled. The sarcomatous character in some parts of a carcinoma could be stimulated by the cells of the carcinoma taking up the shape of mesenchymatous tissue(Ewing, Krompecher, Herzog). A tumor which was found in the uterus of a married woman, 35 years of age, seems to prove the real existence of sarcocarcinomata. The portio of this uterus was changed to an irregular ulcer with exulcerated base. On the right side of the portio a little spherical and firm nodule could be found.

The microscopical examination showed that the exulcerated tumor was formed by a typical squamous cell carcinoma with little tendency to hornification. In the stroma a very intensive inflammatory reaction was to be stated.

In that part of the tumor described above as a spherical firm nodule, the stroma of the tumor consists almost entirely of large spindleshaped cells arranged in fascicles. The nuclei of these spindle cells are large. Mitoses, partly atypic, are very frequent.

Are the spindle cells really cells of the stroma or are they only cells of the carcinoma changed to spindle cells by the pressure of the surrounding tissue? The production of collagenous intercellular material by the questionable spindle cells, the location of the blood vessels exclusively in this part of the tumor seem to suggest that the spindle cells derive from the mesenchyma and that this tumor can be called a sarcocarcinoma.

Concerning the histogenesis of the present tumor it can be supposed that the carcinoma was the primary tumor and that it caused the sarcomatous degeneration of the stroma in which the tendency for excessive growth already preexisted.

March 12, 1923.

FUSIFORM BACILLI AND SPIROCHETES IN TONSILS AND ADENOIDS

I. PILOT AND J. BRAMS

SUMMARY

Fusiform bacilli were found in the extirpated tonsils of eighty-two of 100 children, and in fifteen of forty-six (32.6 per cent.) adenoids. Spirochetes appeared in 25 per cent. of the tonsils especially in large numbers in the actinomyces-like granules. In the adenoids they were demonstrated in only two instances.

Associated with them in both tonsils and adenoids were pyogens—particularly streptococcus hemolyticus and viridans.

In morphology the fusiform bacilli and spirochetes resemble those found about teeth and in certain putrid and gangrenous processes of the mouth and respiratory tract. In the tonsils and adenoids these organisms together with the associated pyogens may be important sources of such infections.

March 12, 1923.

A FORM OF POLYPOID COLITIS AS A LATE STAGE OF AMEBIC DYSENTERY

REPORT OF CASE

LAURENCE E. HINES, M.D.

CHICAGO

History.—A druggist, aged 41, a patient of Dr. W. H. Burmeister, was admitted to St. Joseph's Hospital, Feb. 12, 1922, complaining of diarrhea, rectal tenesmus, weakness, abdominal pain and insomia. He was a native of the United States and had never lived in tropical or other foreign countries. In 1912, he developed a mild diarrhea with from three to five soft stools daily, which persisted in attacks of a mild form for many years with little or no discomfort. In 1917, attacks of severe diarrhea became frequent; the stools became more watery, and numbered from ten to fifteen daily, and occasionally the patient had abdominal cramps. The diarrhea slowly and progressively became worse until, six months before entering the hospital, he was too weak to work. In November, 1921, there was about one-half ounce of blood on the top of the stool, and, after this, blood was noticed frequently. Various diets did not better the diarrhea, although the patient was more comfortable on a diet of soft starchy or carbohydrate foods.

The patient was well developed but poorly nourished, with pale, sallow skin and slightly protruding eyes. There was slight tenderness in the lower left abdominal quadrant. Rectal examination was negative. A blood examination revealed 81 per cent. hemoglobin; 4,450,000 erythrocytes; 10,200 leukocytes; 64 per cent. polymorphonuclears; 26 per cent. small lymphocytes; 9 per cent. large lymphocytes, and 1 per cent transitionals; a Wassermann test of the blood serum was negative. There was a trace of albumin in the urine and a few hyaline casts. He passed from ten to fifteen dark brown, foul, liquid stools daily, all containing large amounts of mucus. No blood was seen grossly, but erythrocytes and leukocytes were observed microscopically; and the Weber test for blood was positive. No amebas were found, although fresh, warm stools were frequently examined. A roentgenogram of the colon after a barium enema showed a pronounced series of small uniform defects, which gave the bowel from sigmoid to cecum a spongy or wormy appearance.

A diagnosis of polypoid colitis was made, and the diarrhea was treated symptomatically with a soft, bland diet, and rectal irrigations of dilute potassium permanganate solution. The patient had been given several intravenous injections of neo-arsphenamin before entering the hospital. No emetin was given at any time. Aug. 14, 1922, a blood examination

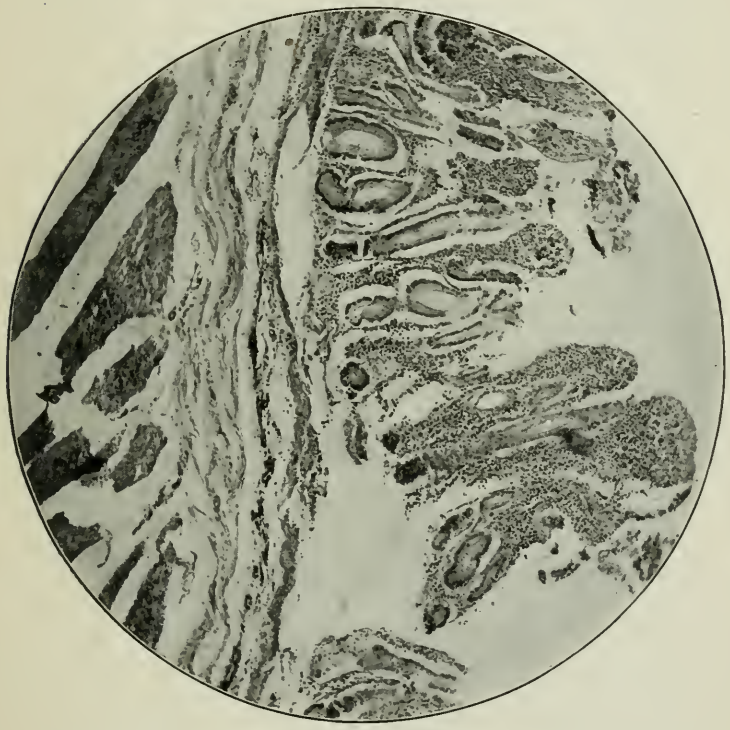

Fig. 1.—Section of colon showing projecting masses of necrotic substance and inflammatory tissue.

showed 41 per cent. hemoglobin, and 3,450,000 erythrocytes. He became weaker and more anemic, and died, August 21.

Necropsy.—This was performed four hours after death. The body was 174 cm. long, and weighed about 125 pounds (57 kg.); it was greatly emaciated; the skin and mucous membranes were pale, and the eyeballs bulged slightly; subcutaneous fatty tissue was scanty; the omentum was attached

by a narrow fibrous band to the sigmoid colon, which was kinked and located high in the peritoneal cavity; there were adhesions between the sigmoid colon and the lateral abdominal wall; the coils of small intestine were free in the peritoneal cavity. The mesenteric lymph glands were slightly

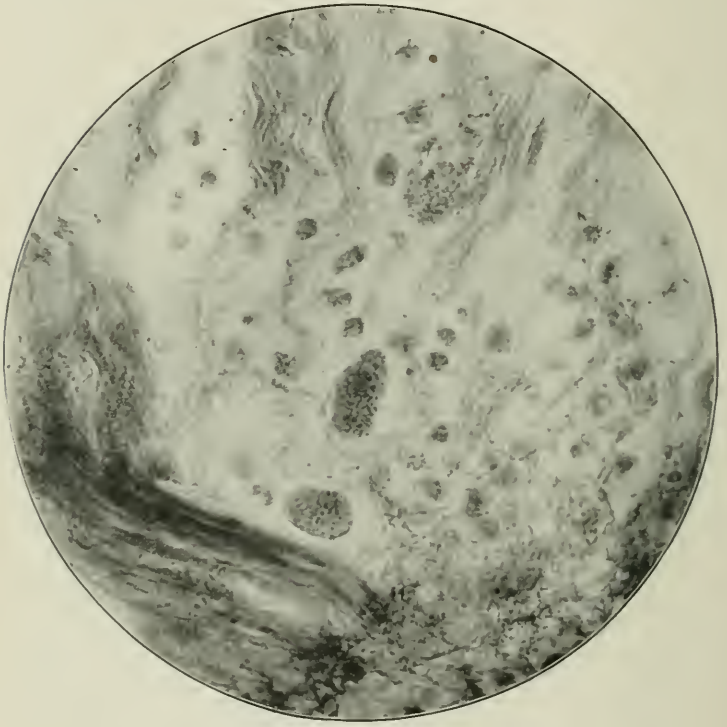

Fig. 2.—Amebas in wall of sigmoid colon.

swollen. The mucosa of the small intestine was slightly congested and covered with mucus, but the wall was not thickened. The wall of the entire colon was greatly thickened, from 4 to 6 mm., in all parts except the portion of kinked sigmoid colon, in which the diameter was from 8 to 11 mm. From the lower part of the ascending colon to the distal part of the pelvic colon, the mucosa was studded with numerous confluent dirty gray nodules. The crescentic folds

(plicae semilunaris coli) were greatly exaggerated, and covered with similar elevations. Some of the nodules projected into the lumen of the bowel 3 mm., while others were flat. The diameter of the nodules varied from 2 to 6 mm., the base usually being about the same diameter as the top. A thick coat of glairy mucus covered the mucosa. In the pelvic colon the nodules were less numerous and discrete, and none were present in the rectum or pouch of the cecum. The elevations in the greatly thickened portion of kinked sigmoid were wider, and submucosal hemorrhages gave the lining a mottled, purple and gray appearance. No recent or healed ulcers could be distinguished grossly in any part of the colon. There were no ulcers or areas of hyperplasia in the mucosa of the esophagus, stomach or small intestine. Other findings were: numerous patches of fatty changes in the intima of the aorta; patchy sclerosis of the epicardium and endocardium; slight atrophy and fatty infiltration of the heart muscle; early sclerotic changes in the kidneys; fibrosis of the spleen, and slight perisplenitis. There were no abscesses in the liver or any gross changes in the pancreas, suprarenals, testes, epididymides or lungs.

Examined microscopically, the nodular elevations of mucosa were composed of granular necrotic material, inflammatory cells and fragments of intestinal glands. In many of the crypts between the nodules, slight ulceration was present. The surface of the nodules was necrotic, and the fragments of intestinal glands, below this layer, showed advanced stages of necrosis, while deeper in the mucosa the outline of the glands was well preserved, but the cells showed varying degrees of degeneration. The lumen of many of the glands contained desquamated epithelial cells and cellular débris. The thickening in most parts of the intestinal wall was due to the cellular infiltration and edema of the mucosa, but in the sigmoid portion much of the thickening was in the submucosa. Plasma cells and lymphocytes were numerous in the stroma of the mucosa, more abundant in the submucosa, and present in small numbers in the muscular coat. Polymorphonuclear leukocytes were seldom found. In the submucosa and inner muscular coat there were many oval and round ameba-like bodies, from 12 to 14 microns in diameter (the plasma cells in this tissue measured from 3 to 5 microns). Some of the bodies were homogeneous and granular with no visible nuclei, while others contained a poorly defined nucleus, eccentrically placed and containing a karyosome-like structure in the center. Red blood cells were present in some of these bodies. Within the epithelial cells of the intestinal glands there were many small deeply stain-

ing bodies from 1 to 3 microns in diameter, some ovoid in shape, others irregular. In some of the glands all the cells contained these bodies; in other glands only a few of the cells contained them, and some were free in the lumen or in the desquamated epithelial cells in the lumen. Some of the bodies were free in the cell, while others were surrounded by a well defined halo. These bodies were somewhat similar to forms of *Endameba histolytica,* which Jackson[1] found in the kidneys of a child and described as vegetative or schizogonic forms.

COMMENT

Polypoid colitis, colitis polyposa, or enteritis polyposa are names applied to adenomatous growths which project or hang by a stalk from the intestinal mucosa. Usually such masses are composed of numerous, irregular, partly cystic glands of greater length than normal glands and embedded in a loose stroma, which, on account of the traumatism to which it is exposed, is constantly inflamed. The growths are often multiple and sometimes so numerous and small as to give the mucosa a shaggy appearance. The polypoid masses in the mucosa of the colon in this case were not adenomatous, but the result of undermining of the mucosa by an inflammatory process. In the process of healing of dysenteric lesions, similar polypoid masses are often formed at the margin of ulcers. Kaufmann[2] calls attention to their presence in tuberculous ulcerative intestinal lesions, and writers on amebic dysentery describe such nodules as a part of the intestinal lesions.

The earliest changes of the colon in amebic dysentery appear as elevations in the mucosa, with a hyperemic or hemorrhagic zone at the periphery and a central plug of yellowish necrotic material. According to Strong,[3] if a small capillary hemorrhage occurs in the elevation, nourishment of the overlying epithelium is disturbed and erosion and ulceration occur: but if there is no hemorrhage, the nodules increase in size through edema and round cell infiltration. The inflammatory process is essentially slow and chronic; few polymorphonuclears are found, while plasma cells

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2. Kaufmann, E.: Spezielle pathologische Anatomie **1**: 512, 1911.
3. Strong, R., in Osler's Modern Medicine **1**: 503, 1904.

and lymphocytes are numerous. The erosions and simple ulcerations usually heal completely or progress to large suppurative, undermined ulcers whose healing is associated with scar formation and contraction.

The appearance of amebas in tissues is apt to be misleading, because they are likely to degenerate quickly after death. Dobell,[4] in his studies on fresh *Endameba histolytica,* describes the typical ones as actively motile bodies from 18 to 40 microns in diameter, with clear cytoplasm, finely granular endoplasm, indistinct, vesicular spherical nuclei, eccentrically placed and containing a central karyosome. As the nuclear characteristics of dead amebas are not clear cut, he believes that the most serviceable criterion for diagnosis is the presence of erythrocytes in the cytoplasm.

The postmortem diagnosis of amebic colitis in the present case is made on the presence in the intestinal wall of bodies morphologically like *Endameba histolytica,* some of which contain erythrocytes. The chronic inflammatory reaction with a large number of plasma cells, which this specimen presents, is the usual finding in amebic dysentery. In amebic dysentery, however, it is unusual to find a colon with no gross signs of ulceration, but with extensive confluent, polypoid masses that give the mucosa a uniformly shaggy appearance. Councilman and Lafleur,[5] Christofferson,[6] Musgrave,[7] Bartlett,[8] Reed,[9] Wooley and Musgrave,[10] and Harris [11] describe the postmortem findings in large series of cases, but no cases were mentioned that were like this one.

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5. Councilman, W. F., and Lafleur, H. A.: Amebic Dysentery, Johns Hopkins Hosp. Rep. **2**: 393, 189, 1891.
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11. Harris, H. F.: Amoebic Dysentery, Am. J. M. Sc. **115**: 384, 1898.

SUMMARY

In a case of amebic dysentery, the colon mucosa presented no gross signs of ulceration, but was the site of multiple confluent polypoid masses.

April 9, 1923.

NEW STUDIES IN ANAPHYLAXIS

W. F. PETERSEN, R. H. JAFFE,
S. A. LEVINSON AND T. P. HUGHES

During the course of experiments in the study of alterations in cellular permeability we have examined changes that occur in the endothelial permeability during acute anaphylactic shock, during intraportal blockade (produced by injecting liquid petrolatum intraportally) and following so-called endothelial blockade. Our experiments were made on normal adult dogs in whom a thoracic duct fistula had been established under local anaesthetic.

(*a*) In acute anaphylactic shock we have observed the following: (1) an immediate increase in the rate of lymph flow, (2) the appearance of red blood corpuscles, (3) incoagulability of the lymph, (4) increase in the phosphates, sugar, total protein, bile pigments, nonprotein nitrogen and the proteolytic enzyme, (5) increase in fibrinogen and the globulins (with small reinjection doses), decrease in the larger molecular aggregates with larger doses of antigen, (6) an immediate increase in the permeability of the endothelium for hemoglobin.

(*b*) That these alterations are not due to an increase in intraportal pressure is made evident when we produce an intraportal blockade by means of oil embolism and occlusion of the hepatic capillaries. An immediate increase in lymph flow takes place, due to the increase in the intraportal pressure but the other changes that we observe in anaphylactic shock do not take place for fully a half hour, i. e., until liver injury, due to the local asphixia, takes place.

(*c*) When the liver endothelium has been blockaded (by the intravenous injection of colloidal iron) ana-

phylactic shock, at least as revealed in the lymph reaction, is modified. There is evidence of considerable protection. Whether this is due to an actual functional blockade of the endothelium is doubtful; it seems more probable that the endothelial elements have been stimulated by the iron injections and are able to dispose of the reinjected antigen more rapidly.

DISCUSSION—PAUL KLEMPERER

The presentation of Dr. Petersen and associates offers me an opportunity to report on our own experiments in which the same methods were applied. These experiments, however, deal with a different phase of immunity. Going out from the fact, that in certain infectious diseases with marked immunological reactions, as for instance, typhoid fever, the reticulo-endothelial cells are greatly increased, therefore I tried to determine whether the antibody formation was changed after injection of colloidal substances which were stored in the reticulo-endothelial system. I experimented on rabbits which were repeatedly injected with trypan-blue, carmine red or saccharated iron. Large amounts of iron proved to be most suitable because there was no reactions following injection. In this way rabbits were intravenously injected on eight succeeding days with 5 c.c. of a 30 per cent. solution of saccharated iron. Afterwards the animals were immunized with either sheep erytrocytes or typhoid bacilli; four to five days after the fourth injection the titer of the serum was determined. There was no difference between the injected and control animals in their hemolytic or agglutination titer.

These experiments, however, were not satisfactory because they are open to several objections. At first the question has to be raised whether it is possible to fill the entire reticulo-endothelial apparatus by the injection of colloidal substances. Secondly whether a function of these cells can be impaired by loading them with iron. To get satisfactory information in regard to the first objection we tried to determine the antibody formation in the spleen. Here we should be

able by histological examination to prove beyond doubt whether the reticulo-endothelial cells were actually loaded or not. Animals were injected in the same way as before, afterwards bled and the spleen washed out with about eight liters of warm Ringer's solution. A piece of the spleen was taken for examination. The pulp and endothelial cells proved to be full of iron granules. The rest of the spleen was ground with sea sand and extracted with physiological salt solution. Neither in these experiments we could find any differences in the antibody titer in injected and control animals.

The only conclusion that could be drawn from these experiments is, that the injection of colloidal substances did not impair the antibody formation. But the main problem, whether the reticulo-endothelial cells do participate in the antibody formation was not touched upon because the question remained unanswered whether a function of these cells could be impaired by a mere mechanical storage process.

FATAL HEMORRHAGE FROM ERODED ARTERIA CYSTICA OF THE GALLBLADDER

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Two acute dangers threaten the life of persons suffering from chronic peptic ulcer: the perforation of the ulcer into the peritoneal cavity, and fatal hemorrhage from eroded blood vessels. Fatal hemorrhages are comparatively rare events in chronic gastric ulcers. Da Costa [1] reports that only 3 to 8 per cent. of persons actually die of hemorrhage. The spread of an ulcer sometimes, though not as often as it is generally considered, causes obstruction of the blood vessels in its base by inflammatory changes in the vessel walls and by thrombosis. In this way larger hemorrhages may be

1. Modern Surgery, 1920, p. 1096.

prevented. But, on the other hand, the contractibility of a blood vessel embedded in the firm, cicatrized tissue of the ulcer may be impaired and so increase the possibility of abundant bleeding from smaller vessels.

My own experience is based on fifty-five cases in which the patients have died from peptic ulcer of the stomach or duodenum. In 41 per cent. of the cases perforation, and in 20 per cent., fatal hemorrhage had occurred.

Sometimes a large hemorrhage of the stomach is produced by the existence of a great many erosions of the mucous membrane, without the opening of a larger blood vessel. In most of the cases, however, a gaping vessel of larger or smaller caliber can be noted in the floor of a peptic ulcer. These eroded blood vessels are in the majority of cases arteries, especially branches of the coronary arteries of the stomach, of the gastroepiploic arteries, or the arteria gastroduodenalis or lienalis. Kaufmann,[2] and Finsterer and Glaessner[3] reported cases in which the ulcer had involved the spleen and led to an erosion of a branch of the lienal artery. Noelle[4] and Morrison[5] observed cases with fatal hemorrhages from the eroded liver. Merkel,[6] in a case of chronic gastric ulcer with abundant hemorrhage, recognized the bleeding blood vessel as the left vena renalis.

A very uncommon and interesting cause of fatal hemorrhage from a chronic gastric ulcer was noted in a necropsy which I performed recently at the request of the attending physician, Dr. Siebel.

A woman, aged about 70, well nourished, died suddenly after she had vomited large masses of blood. At necropsy, the skin was yellowish white; the mucous membranes were very pale. There were only a few livid patches. The lower extremities showed rigor mortis. The peritoneal cavity contained about 1 liter (quart) of dark red fluid blood. The

2. Spezielle pathologische Anatomie **1**, 1912.
3. Mitt. a. d. Grenzgeb. d. Med. u. Chir. **27**: 1, 1913.
4. Inaug. Diss., Greifswald, 1899.
5. Stomach, in Treatise on Regional Surgery **2**: 59.
6. Virchows Arch. f. path. Anat. **173**: 1, 1903.

intestine was distended. Dark red masses filled its lumen, as seen through its wall. The lesser curvature and the adjacent part of the anterior wall of the stomach above the pylorus were covered by, and fixed to, the lower edge of the right lobe of the liver and to the gallbladder. This connection was interrupted on the right and upper side in the region of the gallbladder. A round hole with a diameter of about 1 cm. gaped here. Clots of coagulated blood partly closed this hole. When the stomach was opened, two ulcers were seen just above the pylorus. One of them was located on the posterior surface. It was oval in a diagonal direction, and its diameter amounted to from 1.5 to 2.25 cm. Its shelving edges were indurated, and its floor was formed by the pancreas. The other ulcer involved the lesser curvature and a considerable part of the anterior wall. It was round, with a diameter of 2 cm., and it entirely penetrated the wall of the stomach. Its base consisted, in the lower part, of liver tissue deprived of the capsule and ulcerated; in the upper part, of the gallbladder. The wall of the gallbladder was there changed into a blood-stained ulcer, in the center of which gaped the lumen of an eroded artery. This proved to be the arteria cystica, a branch of the arteria hepatica. The liver was very pale yellowish brown, and firm. The ulcer on its lower edge was oval and smooth, with an almost black vascular injection. The gallbladder contained dark green bile; its mucosa showed no changes.

In the anatomic diagnosis may be noted: fatal hemorrhage from the eroded cystic artery of the gallbladder, the erosion being due to a peptic ulcer of the stomach, that had eroded the gallbladder and the right lower edge of the liver; chronic peptic ulcer of the posterior wall of the stomach; anemia of the organs; emphysema pulmonum; dilatation of the left ventricle of the heart, and a few small sclerotic plaques in the coronary arteries.

April 9, 1923.

THE LIFE CYCLE OF BACILLUS FUSIFORMIS

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The question whether fusiform bacilli and the spirilla with which they are practically always associated, in normal as well as in pathological conditions, are separate organisms or parts of the life cycle of one,

has long been subject for discussion. The earlier workers who reached the conclusion that the two organisms were different forms of one, studied either sections of tissues or mixed cultures. The first pure cultures of fusiform bacilli isolated showed no spirilla. Later in studying pure cultures of these bacilli I found, after a variable incubation period, spiral forms which greatly resembled those seen in smear preparations. They could be overlooked easily as often they were present for only a few days in any considerable number and required special staining. Neither the bacilli nor the spirals could be demonstrated to have progressive motion.

Other observers have found spiral forms in their cultures but some concluded they either were not typical spirilla or that they were dealing with mixed cultures of fusiform bacilli and *Treponema macrodentium* or the *Spirillum sputigeneum*.

Undoubtedly there are several different strains of fusiform bacilli, some of which probably have nothing to do with spirilla.

The present study deals with a pure culture of *Bacillus fusiformis* isolated from a normal tonsil. The material was grown anaerobically first for four days in ascites broth 1 : 3, then subcultures were made on goat blood agar slants. The cultures were repeatedly plated out and colonies well separated in ascites tissue agar to insure a pure culture.

The organism is an obligate anaerobe growing at 36 C. Some body fluid is necessary for growth. The colonies on blood agar are whitish, with a slightly violet tinge, smooth, with regular edges. In fluid mediums the growth is flocculent. A somewhat offensive odor is given off from successful cultures.

Like other strains of fusiform bacilli this one is extremely pleomorphic, forming straight and wavy nonmotile filaments of various lengths, the bacilli and filaments staining blue with Giemsa stain, the bodies inside the organism bright pink, while some of the wavy forms stain bluish pink. It is gram negative but requires thorough decolorization to remove the stain.

After incubation from one to two weeks short spiral forms, 5 microns in length, sharply curved and with pointed ends are observed. They may have from two to ten shallow, regular or irregular curves. They may be single, in pairs or radiate from a central mass. In the dark field they appear granular. When first formed they are actively motile with a progressive, whirling serpentine motion. The body of the spirillum appears flexible. Only one long, fine, wavy flagellum has been demonstrated at the end. The spirilla were found in all the mediums used, but were most numerous on blood agar and in ascites broth to which a small amount of acetic acid was added.

The small spirilla appear to develop in two ways: The bodies inside the threads are occasionally seen to fall out and appear to burst, forming comma forms, then spirilla with from two to ten curves.

The most common method of development of the spirilla seems to occur within the threads. Here also the bodies appear to break up, forming comma shaped spirilla, then spiral forms with from two to four curves until finally the whole filament is filled with spirals with definite, rounded curves of great regularity. The thread may contain spirilla with as many as twenty continuous curves. The spirilla in one filament are generally all at the same stage of development. These spirilla stain bright pink with Giemsa stain, the filaments blue. The spirals inside the thread are distinctly visible when vitally stained with brilliant cresyl-blue and also in the dark field.

In fixed and occasionally in vitally stained preparations, the spirilla may be observed to emerge from the end of the filaments. In some specimens the whole filament appears to dissolve leaving the spirilla free. The spirilla may now increase in length and the curves often become fewer and more shallow. Later they stain irregularly and show inside and outside, in Giemsa preparations, blue, slightly pointed elongated bodies, 2 microns in length, with deeply staining granules at the ends, strongly resembling the short fusiform bacilli seen in early cultures.

As in cultures of other spiral organisms, this one may break up into masses of bodies of various sizes, from which bacilli and threads may be seen to emerge. The masses of bodies may be the symplastic stage described by Löhnis as connecting the different cycles in the life of bacteria, in this instance the spirillar and bacillary stages.

The staining reactions of the spirilla inside the threads and their motility when free speak against their being due to plasmolysis.

The development of new spiral organisms from bodies fallen out of the mother cell or from degenerated spiral cells is well known. There is also evidence that motile organisms may develop inside the cell wall, which later dissolves. Finkler and Prior described this phenomenon in their *Spirillum* and Ferrán made similar observations with cholera spirilla. The formation of motile organisms inside the old cell wall of nonmotile threads has also been described in *Cladothrix dichotoma*.

The development of spirilla from bodies inside the cell wall of fusiform bacilli and the later growth of bacilli from spirilla, tend to confirm the theory that these two organisms are different forms in the life cycle of one.

May 14, 1923.

RÔLE OF OMENTUM OF RABBITS AND DOGS IN ANTIBODY PRODUCTION

PRELIMINARY REPORT

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It has long been known that animals deprived of the omentum are less resistant than normal animals to induce peritoneal infection.[1] Cunningham[2] demon-

1. Buchtel: Denver Med. Times and Utah M. J. **31**: 305, 1911. Hertzler: The Peritoneum, 1919. Wilke: Brit. M. J. **2**: 1103, 1911. Norris: Univ. Penn. M. J. **21**: 119, 1904. Ruhin: Surg., Gynec. & Obst. **12**: 117, 1911.
2. Am. J. Physiol. **59**: 1, 1922.

strated recently that animals deprived of the omentum produced fewer cells of the clasmatocyte type than normal animals in response to peritoneal irritation. The omentum contains many phagocytic cells singly and in islands along the blood vessels, but it has not been determined whether phagocytic action is the only anti-infectious property of the omentum or whether the omentum takes part with the spleen, bone marrow and other organs in the development of antibodies does not seem to be known, and for this reason I have tried to determine by experiments the rôle of the omentum in antibody production.

EXPERIMENTS

The omentum was removed under ether from a series of rabbits and dogs. The operation consisted in the simple excision of this structure after careful ligation of the larger blood vessels as they leave the gastroepiploic vessels along the greater curvature of the stomach. Care must be taken not to interfere with the blood supply of the spleen as the splenic artery passes through the upper border of the omentum. After a period of two weeks for recuperation, these animals were given intraperitoneal injections of defibrinated sheep blood, and then bled from the marginal vein of the ear every two days. Healthy normal rabbits injected and bled in the same way served as controls. After separation the serum was heated at 56 C. for thirty minutes, and then its antibody content determined according to the methods described by Hektoen.[3] For lysin determinations, mixtures were made of 0.2 c.c. of 5 per cent. suspension of washed sheep corpuscles, with 0.003 c.c. of guinea pig serum as complement, and dilutions of inactivated rabbit serum in normal salt solution, so that the total volume in each case was 0.6 c.c. This mixture was incubated for two hours and then placed in the icebox over night. Next morning the highest dilution causing hemolysis was recorded. For precipitin content, the highest dilution of sheep serum in which rabbit serum caused a precipitate by the contact method, after standing at room temperature

3. J. Infect. Dis. **6**: 78, 1909; **19**: 69, 1916.

for one hour, was determined. The agglutinin titers were determined by means of mixtures of 0.2 c.c. of 5 per cent suspension of washed sheep corpuscles and dilutions of inactivated rabbit serum in normal salt solution so that the total volume in each case was 0.6 c.c. The mixtures were incubated for two hours and then placed in an icebox over night, and next morning the highest dilution of each serum causing definite agglutination noted.

REMOVAL OF THE OMENTUM AND INTRAPERITONEAL IMMUNIZATION

The omentum was removed from a series of rabbits as described. Two weeks later under light anesthesia a

TABLE 1.—*Intraperitoneal Immunization of Rabbits Deprived of Omentum*

	Rabbit 2			Rabbit 4			Control Rabbit 1		
Days	Lysins	Precipitin	Agglutinins	Lysins	Precipitin	Agglutinins	Lysins	Precipitin	Agglutinins
2	24	10	0	12	10	0	6	160	0
5	96	80	0	384	40	12	1536	640	96
7	384	320	24	1536	640	96	3072	2560	192
9	768	640	48	3072	2560	192	12288	5120	768
12	3072	1280	96	6144	2560	384	24576	5120	1536
14	6144	1280	96	6144	2560	192	24576	5120	768
16	3072	640	96	6144	2560	96	12288	2560	384
19	1536	640	96	3072	1280	48	6144	1280	192
21	1536	320	48	3072	1280	48	6144	1280	96
23	1536	320	24	1536	1280	48	3072	1280	48
25	1536	320	24	768	1280	24	3072	1280	96
28	768	160	24	768	640	24	3072	640	96
30	384	160	24	384	640	24	1536	640	48
34	384	80	24	384	320	12	768	320	24
37	192	40	12	384	320	6	768	320	24
41	192	20	12	192	80	6	384	80	24
44	192	20	6	192	80	6	384	80	12
50	96	10	6	96	40	6	192	80	12
60	96	10	3	96	20	6	192	40	6
79	0	0	0	48	10	0	96	10	6

small incision was made through the abdominal wall and 15 c.c. of defibrinated sheep blood was introduced. Several controls were immunized in a similar manner at the same time. The rabbits were bled every two days and the concentration of antibodies determined (Table 1).

Two weeks after removing the omentum in a number of dogs 25 c.c. defibrinated sheep blood was

introduced intraperitoneally. Several controls were immunized at the same time in a similar manner. The dogs were bled every two days and a concentration of antibodies in the serum determined as indicated (Table 2). These experiments were repeated several times with similar results.

As seen in the tables the general course of antibody curves corresponds well to that of the typical simple curve following a single antigen injection described by

TABLE 2.—*Intraperitoneal Immunization of Dogs Deprived of Omentum*

	Dog 2		Dog 3		Control Dog 1		Control Dog 2	
Days	Lysins	Agglutinins	Lysins	Agglutinins	Lysins	Agglutinins	Lysins	Agglutinins
1	0	0	0	0	0	0	0	0
3	12	12	12	6	12	12	24	6
5	768	48	384	48	768	96	3072	48
7	6144	192	3072	96	6144	384	6144	192
9	24576	384	12288	192	24576	768	12288	384
12	12288	192	6144	96	12288	384	12288	192
14	12288	192	6144	96	6144	192	6144	96
16	6144	96	3072	48	3072	96	3072	48
18	3072	96	1536	48	1536	96	3072	48
20	1536	96	768	48	768	48	3072	24
23	768	48	768	24	192	48	1536	24
24	384	48	384	12	96	24	768	12
28	192	24	192	6	96	12	192	6
30	96	12	48	6	48	6	96	6
40	96	6	24	0	48	6	96	6
50	48	6	12	0	48	0	48	0
60	24	0	6	0	24	0	48	0
70	24	0	6	0	12	0	24	0

Hektoen and Carlson.[4] The control rabbits produced about four times the quantity of antibodies at the height of the curve as did the rabbits deprived of the omentum, and the active antibody production continued longer in the control rabbits. In the dogs, however, there was no difference in the amounts of lysin and agglutinin in the serum of the dogs without omentum and of the controls.

REMOVAL OF THE OMENTUM AND INTRAVENOUS IMMUNIZATION

Two weeks after removing the omentum from a number of rabbits and dogs 2 c.c. of defibrinated sheep blood was injected into the ear veins. At the same time

4. J. Infect. Dis. **7**: 319, 1910.

control animals were injected in the same way. The animals were subsequently bled every two days and the antibody content of the serum determined. The results from this experiment on rabbits are given in Table 3, which shows that the rabbits deprived of the omentum produced an equal concentration of antibodies in the serum as the control rabbits. The dogs deprived of omentum also produced an equal concentration of antibodies in the serum as the control dogs.

TABLE 3.—*Intravenous Immunization of Rabbits Deprived of Omentum*

	Rabbit 19			Rabbit 20			Control Rabbit 20		
Days	Lysins	Precipitin	Agglutinins	Lysins	Precipitin	Agglutinins	Lysins	Precipitin	Agglutinins
1	0	0	0	0	0	0	0	0	0
3	0	0	0	0	0	0	24	10	6
5	96	20	6	96	20	6	384	160	24
7	768	160	48	768	160	48	1536	320	48
9	1536	640	96	1536	320	96	1536	640	96
11	1536	1280	96	1536	640	96	1536	1280	96
13	768	640	48	768	320	48	1536	640	48
16	768	640	24	384	160	24	768	320	48
17	384	320	12	384	160	12	768	320	24
19	192	160	6	192	80	6	384	160	12
21	96	80	6	96	40	0	192	80	12
23	96	40	0	48	40	0	96	80	6
25	48	10	0	24	10	0	96	40	6
27	24	10	0	12	0	0	48	10	6
30	12	10	0	6	0	0	24	10	0

REMOVAL OF THE OMENTUM AND SPLEEN WITH INTRAPERITONEAL IMMUNIZATION

In a third series of rabbits and dogs, two weeks after removing the omentum, the spleen was removed and defibrinated sheep blood introduced into the peritoneal cavity, 15 c.c. in each of the rabbits and 25 c.c. in each of the dogs. At the same time animals from which only the omentum had been removed as well as suitable normal rabbits and dogs were immunized in a similar manner. The animals were bled every two days and the antibody content of the serum determined. It was found, first, that splenectomy alone produced a definite decrease in antibody production, a result also obtained

by Hektoen,[5] and when splenectomy followed the removal of the omentum there was a more marked decrease than after the simple removal of the omentum.

OMENTAL TRANSPLANTS AND THEIR INFLUENCE ON ANTIBODY PRODUCTION

The omentum was removed from several rabbits and dogs and in two weeks omentum from normal animals transplanted into the peritoneal cavity. In a few the omentum was transplanted in one piece spread over the

TABLE 4.—*Transplantation of Omentum and Intraperitoneal Immunization in Rabbits*

	Transplanted Omentum Rabbit 17			No Omentum Rabbit 18			Normal Control Rabbit 19		
Days	Lysins	Precipitin	Agglutinins	Lysins	Precipitin	Agglutinins	Lysins	Precipitin	Agglutinins
1	0	0	0	0	0	0	12	0	0
2	0	0	0	6	0	0	48	10	6
4	6	0	6	24	10	6	192	20	12
6	192	80	12	384	160	12	768	320	48
8	768	320	24	1536	640	48	3072	1280	96
10	1536	640	24	3072	640	48	6144	2560	192
12	3072	1280	96	6144	1280	196	12288	5120	768
14	3072	1280	48	6144	1280	192	24576	5120	768
16	1536	640	24	3072	1280	96	12288	2560	384
18	1536	640	24	1536	640	48	6144	1280	192
20	768	320	12	768	320	24	3072	640	96
22	768	160	12	384	160	12	1536	320	96
24	768	160	12	384	160	12	1536	320	96
26	384	80	6	192	80	12	1536	320	96
28	384	80	6	192	80	6	1536	320	48
30	192	40	6	192	80	6	768	160	24

abdominal viscera. In others the omentum was cut into small pieces of about 1 square centimeter and inserted. The animals were killed at the end of two weeks and the omental transplants studied histologically. It was found that in both methods of transplantation the omentum became converted into acellular fibrous masses which were adherent to the peritoneum.

In similar series defibrinated blood was injected at the time of transplantation of the omentum and the antibody content determined. The results from omental transplantation are given in Table 4 which shows that rabbits with transplanted omentum did not produce more antibodies than rabbits deprived of the omentum, both giving less than the normal controls.

5. J. Infect. Dis. **27**: 23, 1920.

SUMMARY

Rabbits deprived of omentum produced about one-fourth as high a concentration of antibodies in their serum as normal rabbits, subsequent to intraperitoneal immunization, whereas dogs deprived of omentum produced about the same amount as normal dogs. In order to try to explain this difference, I studied the omentum of rabbits and dogs. The rabbit omentum has a different structure than that of the dog. The most characteristic elements of the rabbit omentum are the cellular islands ("taches laiteuses") scattered throughout, usually along the smaller arterioles and capillaries, although many have no demonstrable vascular connections. The cells in these areas are chiefly of the endothelial type, a variety which has received many names, such as "endotheliocyte" by Foot,[6] "macrophages" by Maximow, wandering macrophages, phagocytes, plasmatocytes, etc. One of the essential properties of these cells is to take up vital stains and phagocytize particulate matter from the peritoneal cavity. The cellular aggregations closely resemble in structure the Malpighian bodies of the spleen and may have a similar function.

The omentum of the dog consist chiefly of a vascular network between two serous surfaces. The vascularity is more extensive than in the rabbit but there are no distinct cellular islands, the only endothelial cells present occurring along the blood vessels.

The omentum in the guinea pig, rat, human fetus is similar in structure to the omentum of the dog.

On intravenous injection of the antigen there was no marked difference in the amounts of antibody produced in the animals with and without the amentum. This indicates that the variation in the experiments with intraperitoneal immunization in the rabbit was dependent on some local reaction of the omentum.

6. J. Exper. M. 34: 625, 1921.

CONCLUSIONS

The omentum of the rabbit takes part in the development of antibodies, but the omentum of the dog apparently has no such function. This difference is probably due to the difference in structure of the omentum in the two species, the rabbit omentum containing islands of endothelial cells which may take part in forming antibodies especially on intraperitoneal injection of the antigen.

Transplanted omentum soon is converted into fibrous tissue devoid of endothelial cells.

May 14, 1923.

AN UNUSUAL FORM OF ULCERATION OF THE STOMACH

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The patient, a male, aged 40, was admitted with a provisional diagnosis of carcinoma of the stomach. He had pain after meals, marked loss of weight, vomiting, a hard tumor mass in the abdomen and anacidity of the stomach contents. There was also a positive Wassermann test on the serum of the blood.

Death occurred in five days after admission and the autopsy revealed a stomach which was free from malignancy. The mucosa was atrophic and showed five, shallow, irregular, large ulcers which reached to the muscularis mucosae. The pylorus was markedly thickened and the opening was narrowed. The thickening was due to an hypertrophy of the inner muscular layer at this region. No inflammatory changes could be seen at this place.

The shallow ulcers which may be more properly called erosions were of the mucosa only. The bases and sides were of a round cell infiltration which was covered by a coating of fibrin and necrotic tissue. The

margins were distinct but not thick or undermined. Various bacterial stains were made but no bacteria were found. The Levaditi stain for spirochetes was also negative.

In view of the absence of pathologic changes elsewhere in the abdomen it was considered that the primary condition was the pyloric hypertrophy which was probably of so-called idiopathic origin. The fragile mucosa made this layer susceptible to any mechanical injury as from the retained food particles. The resulting erosions further increased the pylorospasm thus forming a vicious circle.

Seven reports of idiopathic hypertrophic pyloric stenosis in adults were found in the literature. The condition is supposed to be the expression of a motor neurosis or other nervous disturbance. No other cause for this marked pyloric spasm and hypertrophy could be found in the case reported.

May 14, 1923.

PRIMARY SPONTANEOUS TUMORS OF THE UTERUS IN MICE WITH A REVIEW OF THE COMPARATIVE PATHOLOGY OF UTERINE NEOPLASMS

MAUD SLYE, HARRIET F. HOLMES
AND
H. GIDEON WELLS

ABSTRACT

A review of the literature on the comparative pathology of uterine tumors emphasizes the great infrequency of such growths in all the lower mammals, as contrasted with the high incidence in man, and even in proportion to other sites in the lower mammals. This is particularly noteworthy in view of the great frequency of mammary gland carcinoma in some species, and of ovarian tumors in other animals. Of all lower mammals uterine cancer is least rare in cows, but even in this species it is far from common and constitutes

but a small proportion of all the bovine neoplasms. Even in dogs, susceptible as they are to tumor formation, uterine carcinomas are almost unknown. A few cases have been described in wild animals. Leiomyomas are observed perhaps a little more frequently than carcinomas, but they are remarkably uncommon in view of their great frequency in the human female. Only in rabbits are uterine tumors at all numerous, and this because one observer, Stilling, had thirteen cases in a single strain of rabbits under his observation, an observation supporting the experience of this laboratory that heredity may determine not only the frequency but also the site and character of tumor formation.

In mice but few uterine tumors have been described. In the literature we can find records of but three, two fibromyomas and one carcinoma. They are also very rare in the Slye stock, for in 39,000 autopsies we have found but twenty-two animals with unquestionable primary uterine tumors, of which eleven were leiomyomas, seven sarcomas, three adenomas and one teratoma. The leiomyomas were all rather small, and exhibited quite the same character as in the human uterus, with the same tendency to hyalinization and calcification; in none did we observe any malignant transformation. The sarcomas were of different types, some spindle cell and others with comparatively large polyhedral cells, these growths resembling somewhat the "mesotheliomas" of the urogenital tissues. Two of the adenomas exhibited a diffuse infiltration of the entire uterine wall, suggesting malignancy, but the histological characters resembled those of the human adenomyomas. There was also a carcinoma filling the vagina which may have arisen in the cervix. With these possible exceptions there were no cases of carcinoma of the uterus, either primary or secondary, in all these 39,000 mice, despite the great number of other neoplasms among them. Neither was anything found resembling a syncytioma, either in the uterus or elsewhere.

(The complete paper will be published in the Journal of Cancer Research.)

May 14, 1923.

GROWTH OF TISSUE IN VITRO

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Since Harrison first described the cultivation of tissues outside the body in 1907, there has been a considerable amount of work done in various laboratories but chiefly by workers in the Rockefeller Institute, which has shed light on many factors of cell growth.

It is my purpose briefly to outline the nature and result of this work and to present some of my own.

Burrows and Carrel in 1910 undertook to cultivate various kinds of tissue following methods slightly modified from those described by Harrison. They succeeded in growing arterial sheath, con. tissue, cartilage, peritoneal endothelium, bone, epidermis, thyroid, spleen and kidney tissue. The method of cultivation consisted in implanting small bits of tissue in homo or autogenous plasma on a cover slip and inverting this over a ground glass slide. The plasma coagulates quickly and imbeds the tissue firmly. After a period of from ten hours to two or three days at 37 degrees depending on the age of the organism and type of tissue, new growth occurs. Since that time modifications in the cultural environment have been made and the influence of different factors on growth have been discovered, the chief of which follow:

1. Rat sarcoma and normal spleen were found to grow to a slight degree in heterologous plasma, viz., mouse, guinea pig, rabbit, dog and pigeon.

2. Foetal tissues have great inherent power of growth and will grow in heteroplasmic media, Locks solution plus 2 per cent. agar, or in semi fluid media when a support such as silk veil is used.

3. An extract of homologous foetal tissue added to plasma greatly increases the growth of adult tissues.

4. Tissues may be stored in the icebox in Ringer's solution and grow after six or seven days. The optimum temperature of storage is 6 C.

5. Tissues tend to reproduce type and configuration of original tissue e. g. carcinoma grow out in flat sheets, glandular tissue in acinar formation.

6. By transplanting tissue at frequent intervals, two and seven days, and using embryonic tissue or extract added to older tissue, growth of fibroblastic tissue has been continued successively for over ten years.

7. Pure cultures of various types of cells may be isolated and grown from old cultures. In this way fibroblasts, epithelial cells and recently large mononuclear leucocytes and cartilage cells have been isolated and grown.

8. Human tissue is difficult to grow on account of liquefaction of the coagulated plasma but has been successfully accomplished. Chicken plasma added to human plasma prevents liquefaction of growing human sarcoma.

9. Bacteria grown with tissue show a rough parallelism with the virulence of organism for animal supplying the tissue i. e. *B. diph, coli* and *typh.* grow but not *B. prodigiosus.*

10. Multiplication and rate of multiplication of fibroblasts in vitro is due to embryonic juice but food for growth is taken from plasma.

11. Vacuolization of cells in vitro occurs before growth stops and is hastened by *B. typh.* growing with tissue. Dextrose added to media in .5 to 1 per cent. delays vacuolization.

12. Nerve cells grow well with production of long axis cylinders; when these are cut degeneration of peripheral end and regeneration from central end may be observed.

Tissue growth in vitro offers great possibilities of studying the mechanism and site of formation of immune bodies. It is with this phase of the subject that I have been especially interested. Carrel and Ingebrigsten in 1912 found that hemolysins could be produced in vitro when goat blood was added to growing guinea-pig bone marrow and lymphglands. Phagocytosis of red blood cells was observed. Phagocytosis

was observed in con. tissue, endodermal membrane and mesothelium from chick when *B. typhosis* was added. Fischer found that a small amount of foreign protein added to culture medium does not modify the rate of proliferation of fibroblasts but large amounts of foreign protein inhibit the growth except when tissue has been used that has been grown in small amounts of the foreign proteins, i. e., in which the culture has been immunized against the antigen.

Personal observations that have been published have shown that foreign red blood cells introduced into rabbits are taken up by fixed phagocytic cells of the liver and spleen and that in these organs, by a suitable method of extraction, hemolysins can be shown in greater concentration than in the blood stream. The presumption is very strong that the antibody is formed in these phagocytic cells. It was thought that this might be proven by tissue culture methods. Accordingly rabbits were immunized to sheep blood cells and then the antibody in the animals serum permitted to "run down" by allowing a two or three months' rest period. These animals were then exsanguinated and the liver and spleen cultured in the plasma of normal rabbits. To some of the cultures, in a large hanging drop prepared by a glass plate sealed over a watch glass, small amounts of washed sheep red blood cells were added while others were kept as controls under identical conditions. It was hoped that the cells—previously sensitized by the foreign cells would respond by the production of antibody without a latent period. The tissues in most instances showed definite signs of growth within forty-eight hours and the maximum was obtained at four or five days. At this time the coagulated plasma and tissue was ground up in sterile salt solution using the weight of the implanted tissue as equivalent gram for gram with the blood serum. The extracts were then titrated with sheep red blood cells and the results recorded. Six rabbits treated in this manner with about fifty cultures are represented. The following results were obtained:

1. Before growing the tissues, the hemolytic titer was always greater in the serum of the immunized animal than in the extract of the liver and spleen.

2. After incubation for four or five days with growth of tissue but without the addition of antigen, the titer of the spleen extract usually equalled that of the serum of the immunized animal and was greater than that of the animal from which the plasma was obtained. This probably indicated more efficient extraction after incubation than before. Extract of the liver growing in vitro without antigen showed quite constant non-specific hemolysis, i. e., hemolysis without activation by complement.

3. The addition of antigen to the tissue delayed the growth of the tissue but did not stop its growth altogether. The addition of embryonic rabbit extract greatly increased the growth of the tissues but did not increase antibody production.

4. With antigen added to cultures there was definite specific antibody, produced by liver. In one case there was ten times in another two times the amount of antibody in the spleen with antigen as that without antigen.

5. It may be concluded that antibody to sheep red blood cells may be produced in vitro by growing sensitized tissues with specific antigen. The type of cell responsible for this antibody was not determined. It will probably be necessary to grow the various type cells in pure culture before this can be definitely proven.

May 14, 1923.

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